INCIDENTAL FINDINGS IN LIVER AUTOPSY

A DISSERTATION

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CERTIFICATE

This is to certify that this dissertation entitled **"INCIDENTAL FINDINGS IN LIVER AUTOPSY"** is a bonafide work done by **Dr.P.JAYAGANESH**, in partial fulfillment of the regulations of The TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY, Chennai for the award of M.D. Pathology Degree.

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I declare that this dissertation entitled **"INCIDENTAL FINDINGS IN LIVER AUTOPSY"** has been done by me under the guidance and supervision of **Prof.Dr.N.SHANTHI VIJAYALAKSHMI, M.D.,** It is submitted in partial fulfillment of the requirements for the award of the M.D., Pathology March 2008 Examination to be held under The Tamilnadu Dr. M.G.R. Medical University, Chennai. This has not been submitted by me for the award of any degree or diploma from any other University.

Dr.P.JAYAGANESH

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CONTENTS

Introduction

INTRODUCTION

Autopsy remains one of the most useful tools to validate clinical diagnosis. Silent liver diseases are not uncommon and histology is the unique method for diagnosis of silent liver diseases. Autopsy serves to unravel the alterations in liver pathology due to many factors such as alcoholism, infections mainly of viral origin, drug related and neoplasms.

Due to the resurgence of radiological methods, gene tests and molecular studies, the number of liver biopsies done have been reducing in number now a days. Most of the diseases come to the light of the clinician only during autopsy. The effects of viral hepatitis and drug related toxicity to liver is evident only in post mortem studies as liver biopsies are seldom done in these cases.

Hepatitis B has become very prevalent and an estimate of about 350 million people world wide is chronically infected with HBV. Hepatitis B carriers are monitored so much because of the increased risk of cirrhosis, hepatic decompensation, and hepatocellular carcinoma in them. Although most carriers will not develop hepatic complications from chronic hepatitis, 15% to 40% will develop serious sequelae during their lifetime.[4]

Orcein staining can be used as a simple method to study the occurrence of hepatitis B carriers in autopsy material. It was identified in a study of occurrence of hepatitis B surface antigen in

a consecutive material of liver biopsies that Orcein staining of ground glass hepatocytes was a highly specific HBsAg marker. The sensitivity was about 80% in cases with minimal changes, chronic hepatitis and cirrhosis.[50]

Fatty liver disease that develops in the absence of alcohol abuse is recognized increasingly as a major health burden. Since there are no strict guidelines to indications for biopsy in these cases, autopsy can be a useful mode in assessing Non alcoholic fatty liver disease.[10]

AIMS and OBJECTIVES

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1) To study the spectrum of histomorphological features those are commonly observed in liver in different age groups and sex in autopsies.

2) To study the morphological types of Hepatitis of varying Etiologies in Autopsy Study.

3) To study the random occurrence of hepatitis B in 100 Autopsied livers using the method of Orcein stain in general population.

4) To compare the present study with the available references.

REVIEW of LITERATURE

REVIEW OF LITERATURE

Post mortem examination has evolved through a protean range of interest but remains a bench mark in the study of human disease.

It has been performed for thousands of years but it was until the 18th century that they became recognized as being fundamental to medical practice. Autopsy remains one of the most reliable methods to validate clinical diagnosis.

Greek physicians performed autopsies 2500 years ago. An autopsy on the oldest body, an Egyptian mummy 3200 years old has been reported by a team of scientists from Toronto, Detroit, Philadelphia & Cardiff. They demonstrated cysts of Trichinella spiralis, species of taenia and calcified ova of Schistosome in Liver, Kidney, large & small intestine.

The two great 19th century Medical researchers, Rudolf Virchow and Karl Von Rokitansky built on the Renaissance legacy to derive the two distinct autopsy techniques. Their demonstration of correspondences between pathological conditions in dead bodies and symptoms and illness in the living opened the way for a different way of thinking about disease and its treatment .[38] Terry et al, in the year 1955, suggested needle autopsies to be the best for studying liver autopsies.[4]

In a study of 394 consecutive needle autopsy cases, pathological alterations were found in

more than 77%. However in another study by West M. Chomet et al discrepancies between the results of needle autopsies and subsequent complete autopsies were found in only 52% of cases.[51]

Liver is the site of many diseases many of which become symptomatic while some are diagnosed only in autopsy.

Alcoholism & Alcohol related liver disease constitutes the largest health problem in India.

Archaeological records of the earliest civilization show that the history of alcohol dates back over 50,000 years. Alcohol related diseases were recorded in ayurveda written about 567 years BC.[36]

Numerous reviews on the pathology and pathogenesis of alcohol associated liver injury has been published by MC.Sween, Maddrey WC, Rabin and Ishak et al.[23, 29]

The Possibility of Genetic and acquired factors playing a role in the susceptibility of the individual to alcohol associated liver disease is relatively a new concept and has been reviewed by Saunders et al, Sorensons , et al.[45]

The spectrum of alcoholic liver disease includes steatosis, perivenular hepatitis, occlusive venous lesions, cirrhosis and Hepatocellular carcinoma.

Nonalcoholic fatty liver disease is now recognized as a clinicopathological entity that extends beyond uncomplicated steatosis to steatohepatitis, Steatonecrosis and liver cell failure. The term NASH was introduced by Ludwig et al to describe an alcoholic hepatitis like injury

occurring in the livers of Non-alcoholics.[28]

Adler H. Schaffner et al and Nasrallah SM et al, described similar hepatic lesions in obese patients who had neither abused alcohol nor undergone weight loss surgery.[2, 33]

In a study by Eldar'A', Schaffer M., NASH was found in up to 0.6% of autopsy cases.[19]

The transmittable nature of hepatitis through blood transfusions and syringes was found in 1885 when epidemics of jaundice broke out during the wars of the 17th –19th century.

In 1947, Mc.Callum et al classified viral Hepatitis into 2 types – viral Hepatitis A or infectious hepatitis and viral hepatitis B or serum hepatitis. By 1963, research concerning Hepatitis finally paid off.

In 1965, Baruch Blumberg et al discovered the Australian Antigen (Later known to be Hepatitis B surface antigen) in the blood of arborigenes.

In 1970, Dane et al discovered the Dane particle and in 1972 Magnus et al discovered HBeAg.

De Groote J, Desmet V et al in the year 1968 classified chronic hepatitis in to chronic persistant hepatitis and chronic active hepatitis. In two recent editorials published by Scheuer P et al and Gerber et al, reassessment of the nomenclature was done and this classification covers chronic hepatitis as a spectrum of common inflammatory reaction, the histological presentation of which oscillates in grade, may be modified by structural alteration such as fibrosis or cirrhosis and may have different prognostic and therapeutic implications according to etiology.[39].

The Clinical entity - Cirrhosis was identified by the first anatomic pathologist Ganbattista Morgagne in his 500 autopsies published in 1761 but the name cirrhosis was coined by Rene Laennac et al in the year 1826.

Leevy S.M Anthony P and Ishak et al classified cirrhosis morphologically into micronodular, macronodular and mixed nodularity. This Morphological classification is of great value in autopsy studies of the whole liver.[4]

Special stains can be helpful adjuncts in studying various diseases of the liver. Perls' stain on liver sections provides valuable information about the level of iron stores. Pearse A.G.E et al in 1972 recommended the Perls' technique in detecting both Ferritin and haemosiderin, because of its high degree of sensitivity and specificity.[35]

Richter et al in the year 1978 found out that, Ferritin dispersed through the cell sap produces a diffuse bluish tint to the cytoplasm, Whereas intense blue granules correspond to Ferritin and haemosiderin stored together within siderosomes using Perls stain.

In the year 1987, Searle J.W and Ken J. F .R et al described criteria for histological grading of iron storage (after review of many studies). The advantage of this system was that iron in all cell types in the liver was included in the assessment, no subjective estimation of the percentage of cells containing iron was required and the magnification used to make judgment about the amount of iron visible was specified.[30]

The grading system takes in to account the presence or absence of granules at a given magnification. Grade 0 denotes absence of granules at 40x and Grade 4+ denoting visible

masses at 10x or naked eye, with 1+, 2+ and 3+ being intermediate.[30]

Grade 0 & 1+ being within normal limits corresponding to chemically estimated tissue iron concentration of 5-40 umol/ dry wt

Grade 3+ and 4+ represent significant increases in hepatic iron concentration (130-850 umol/g dry wt)

Grading of 2+ is suggestive of mild iron overload, practically if haemosiderin is found almost exclusively in parenchymal cells.

The valve of PAS in detecting hepatic glycogen has been reviewed by Sheehan DC & Luna L.H et al.[41]

The liver cell is rich in glycogen but in routine H & E preparation, its presence is discerned only with difficulty imparting a reticulated and foamy appearance to the cell cytoplasm. Staining by the PAS method readily demonstrates the glycogen and it is uniformly distributed.

Scientists had postulated the association between HBV and HCC based on ecological comparison studies but were initially unable to demonstrate the virus within the HCC tissue until 1970, when a Japanese pathologist Shikata developed a histochemical stain called orcein stain which could stain the HBsAg with in the tissue and thereby allowing the identification of the virus in liver tissue.

In the year 1979, F. Borchard and V.Gursman of the university of Dusseldrof federal Republic of Germany conducted a study for detection of HBsAg containing cells in liver biopsies by different stains like Orcein ,

Aldehydethionine and Chromotrope aniline blue and classified positively reacting ground glass hepatocytes (GGH) into V Grades.[8]

Type I showing a positive staining of cytoplasmic periphery (marginal GGH), Type II showing a diffuse staining(Diffuse GGH), Type III showing globular positive cytoplasmic masses (Globular GGH), Type IV showing spotty drop like positive structures and Type V featuring positive staining ground glass hepatocytes with fatty changes .[8]

In all carriers and patients with minimal hepatitis – GGH mostly Type I &II appeared in extensive clusters within the lobules.

In chronic persistent hepatitis there were moderately numerous, partly grouped partly disseminated GGH of type II & III.

In Chronic active hepatitis, there were only a few GGH of Type IV.

In acute viral hepatitis there were no typical GGH, however positively stained phagocytes were seen. Single so called metabolic GGH sometimes showed similar pictures, however they could usually be distinguished from virus containing GGH because of their granular cytoplasmic structure and lower staining intensity.[8]

Among the three stains, the Orcein stain yielded the best results.

Kostich ND, Ingham CD et al studied on detection of hepatitis B surface antigen by means of Orcein staining of liver biopsies from 65 patients and

16 autopsies by modified Shikata orcein method .They found it useful in cases of chronic hepatitis, detecting asymptomatic carriers, and also in determining the etiology of cirrhosis.[26]

Studies on liver autopsy were done by some authors to reveal the silent lesions in liver histology which were mostly asymptomatic in the living state.

A study conducted by Bal M S, S.P. Singh et al on pathological findings in liver autopsy in 2004 revealed in 100 cases the following findings.

39% had fatty change, 30 % with normal histology, 14% with cirrhosis, 9 % showed congestion, 3% with hepatitis and 3 % showed evidence of malignancy.[6]

Another study conducted by Ghazala Hanif, Abdul Hannan Nagi et al was on incidental findings in the liver in autopsy of 110 cases in 2001 which revealed the following findings.

62.7% showed normal histology, 37.3% showed different liver diseases with 12.7% with chronic hepatitis, 4.5% cirrhosis, 4.5% fatty change, 2.7% venous congestion, 0.9% tuberculosis and 10.9% of non specific reactive hepatitis.[22]

Another study was done in Tehran on silent lesions in liver autopsy in 896 cases in a span of 2 years by Sotoudehmanesh R, Sotoudeh M et al in 2006 and it revealed the following

467 showed normal histology (52.1%) , 283 showed features of steatosis (31.6%) , 19 showed features of steatohepatitis (2.1%), 23 showed features of chronic hepatitis(2.6 %) and 7 cases of cirrhosis(0.8%).[46]

We shall review the different entities that can be commonly encountered in liver during autopsy studies.

PASSIVE CONGESTION AND CENTRILOBULAR NECROSIS

These hepatic manifestations of systemic circulatory compromise are considered together because they represent a morphological continuum. Both changes are commonly seen at autopsy, because there is an element of preterminal circulatory failure with virtually every death.[13]

Right sided cardiac decompensation leads to passive congestion of the liver.

The liver is slightly enlarged, tense and cyanotic with round edges. The liver takes on a variegated mottled appearance, known traditionally as the 'Nutmeg' Liver. Microscopically, there is congestion of centrilobular sinusoids.

Left sided cardiac failure or shock may lead to hepatic hypoperfusion and hypoxia. The hepatocytes in the central region of the lobule undergo ischaemic necrosis centrilobular necrosis is visible microscopically as slight depression of necrotic lobular centers. By microscopy there is a sharp demarcation of viable hepatocytes in the periportal region versus necrotic hepatocytes in the centrilobular region of the parenchyma. Congestion alone no matter how severe or prolonged seems to do little if any damage to the liver. Centrilobular necrosis or ischemic hepatitis appears to result from hepatic hypoperfusion and mimics viral hepatitis.[32]

ALCOHOLIC LIVER DISEASE:

Alcoholism is a leading cause of liver disease. Worldwide risk for severe hepatic injury

correlates with daily intake, with intake of at least 80g of alcohol per day a risk factor for severe hepatic injury.

However only 10% to 15% of alcoholics develop cirrhosis

Three forms of Alcoholic liver disease are recognised:

1. Hepatic steatosis
2. Alcoholic steatohepatitis.
3. Cirrhosis

Hepatic steatosis:

Fatty liver (steatosis) is a common histological finding in liver biopsies which is most often attributed to the effects of alcohol excess but also to obesity, diabetes or drugs. It was seen in up to 90% of patients with chronic alcoholism in a study conducted by Edmondson H.A & Peters R.L et al.[17]

Sudden death may occur in alcoholics whose liver shows severe fatty changes in autopsy.

Pathological features:

Gross findings:

The liver in steatosis is enlarged, yellow, soft and greasy. Fat may be irregularly distributed.(Fig 4)

Microscopic findings:

Although the distinction is not always sharp, steatosis can be subclassified in to two morphological categories macrovesicular and microvesicular.

Macrovesicular steatosis:

Most affected hepatocytes contain a single, large, rounded vacuole that displaces the nucleus and cytoplasm to the periphery of the cell. Fatty change occurs predominately in zone 3 of the liver acinus and is seen

initially in hepatocytes adjacent to the terminal hepatic venule. It spreads from there to involve hepatocytes in all zones.

Mostly steatosis is perivenular but periportal steatosis is sometimes seen in AIDS, in patients on parenteral nutrition and in kwashiorkor. In patients with diabetes mellitus, glycogen vacuolation of hepatocyte nuclei is common.[1]

Macro vesicular steatosis is typically associated with a more long standing disturbance of hepatic lipid metabolism and has, until recently, been considered a benign condition.[16] There is now little doubt that macrovesicular steatosis of both alcohol and non-alcohol related etiologies is associated with the development of more advanced disease: necroinflammation (steatohepatitis) , fibrosis and cirrhosis.[16]

Microvesicular steatosis:

Generally connotes a more serious injury than macrovesicular steatosis, although it has been shown that this is a frequent non specific finding especially in autopsy material by Fraser J.L and Antonioli DA et al.[20]

Hepatocytes with microvesicular steatosis show a central nucleus surrounded by sharply defined small vacuoles.

In autolysed autopsy specimens, the cytoplasm can have a clear appearance and the vacuoles might not be readily discernible.

Microvesicular steatosis is also seen in REYEs syndrome, acute fatty liver of pregnancy, alcoholic liver injury (alcoholic foamy degeneration) and drug induced (salicylates or valproate).[43]

Epidemic delta virus superinfection of chronic hepatitis B is dominated histopathologically by microvesicular steatosis.

The fatty change can be quantified as per Sherlock as 1+ denoting less than 25% of liver cells containing fat, 2+ denoting 25-50% of liver cells containing fat, 3+ denoting 50-75 % of liver cells containing fat and 4+ denoting more than 75 % of liver cells containing fat.[42]

STEATO HEPATITIS:

Beckett et al used the term acute alcoholic hepatitis to describe a clinicopathologic syndrome. Since alcoholic hepatitis may be asymptomatic and up to 39% of patients have established cirrhosis at the time of first presentation, true incidence of alcoholic hepatitis remains to be determined.[30]

Gross appearance:

The liver in alcoholic hepatitis is variable. The Liver is often enlarged and steatotic, with increased fibrosis imparting a firm texture.

Microscopic Findings:

It has four characteristic features:

1. Hepatocyte necrosis and ballooning degeneration. Hepatocytes are swollen with pale staining, finely granular cytoplasm. Apoptotic bodies may be present but are less conspicuous.
2. Mallorys hyaline consisting of tangled intermediate filaments and appears as eosinophilic ropy cytoplasmic inclusions usually in a perinuclear location in hepatocytes undergoing ballooning degeneration.
3. Neutrophil infiltrate – Polymorphonuclear cells are present in small clusters in the lobule and are commonly found surrounding ballooned hepatocytes containing Mallorys hyaline. A portal lymphocytic infiltrate may be seen but is not a prominent feature.
4. Centrilobular pericellular and sinusoidal fibrosis. Delicate strands of collagen surround centrilobular hepatocytes in a chicken wire pattern. As fibrosis progresses, central – portal fibrous bridges form, eventually resulting in micronodular cirrhosis.[30]

Giant mitochondria may be seen on light microscopy as eosinophilic globular and occasionally needle shaped cytoplasmic inclusions, the presence of which may be a diagnostic hint of chronic alcohol consumption.[52]

Sclerosing hyaline necrosis forms a part of the spectrum of alcoholic hepatitis, featuring extensive degree of perivenular liver cell necrosis and fibrosis.[18]

Chapman RW and Morgan MY et al studied about the hepatic iron stores and markers of iron overload in alcoholics and observed that in one third of chronic alcoholics, there was a increase in the hepatic iron concentration.

CIRRHOSIS:

In alcoholic cirrhosis, the liver is enlarged in early stages with a finely granular capsular and cut surface.

The texture is firmer than normal.

Micronodular cirrhosis is the most common type of cirrhosis seen in alcoholism. As the cirrhosis progresses, a mixed macro and micronodular pattern may be seen. Broad expanses of Fibrous scar are commonly seen. Mallory's hyaline is usually not seen.

Burt et al in a retrospective autopsy & biopsy study observed occlusive venous lesions in alcoholic liver disease.[12]

FIBROSIS:

Fibrosis is occasionally seen in alcoholics in the absence of severe steatosis or steatohepatitis.

Perivenular fibrosis may be found with or with out steatosis or Steatohepatitis.

Pericellular fibrosis is an important component of steatohepatitis. Morgan M.Y, Sherlock S,Scheuer P.J observed portal fibrosis in the liver of alcoholics in their study.[42]

Siderosis is quite common in the livers of drunkers, but is usually mild and involves Kupffer cells as well as hepatocytes. It is said that a grade of 1+ /2+ is only alcohol related and in patients with alcoholic liver disease, a grade of 3+ /4+ is thought to be related to genetic haemochromatosis.[37]

Severe cholestasis has also been described in association with fatty liver, alcoholic foamy degeneration, alcoholic hepatitis and alcoholic cirrhosis.

NON ALCOHOLIC STEATO HEPATITIS (NASH)

NASH or Non alcoholic fatty liver disease (NAFLD) is rapidly emerging as the most common liver disease and encompasses a wide spectrum of pathologic changes ranging from simple steatosis at one end to steatohepatitis, fibrosis and cirrhosis at the other.[10]

According to Neuschwander, Tetri.B.A Caldwell SH et al, in patients with risk factors for NAFLD like obesity and TYPE 2 Diabetes , it is estimated that

50-70% showed steatosis, 20-30% progress to steatohepatitis and 2-3% develop cirrhosis.[10]

Risk factors include female gender, obesity, rapid weight loss and type 2 DM.

Gross findings:

Liver is enlarged, soft, and yellow with greasy texture due to lipid accumulation. Fat may be decreased in later stages, especially in cirrhosis due to NAFLD.

Microscopic findings:

The histological features mimic alcoholic hepatitis although the injury tends to be less severe and Mallory bodies may be sparse or absent.

1. Steatosis:

The fat occurs in macrovesicular or mixed patterns, steatosis is present in nearly 100% of cases.

2. INFLAMMATION:

Mild mixed acinar inflammation is considered the hallmark of steatohepatitis. Neutrophils

usually in small numbers, can surround the

ballooned hepatocytes (satellitosis) mild acinar and portal mononuclear inflammation including lymphocytes and histiocytes is also common.

3. Hepatocellular injury is a prerequisite for the diagnosis of steatohepatitis. Evidence of Hepatocellular injury most often occurs in the form of hepatocellular ballooning or pericellular fibrosis.

The minimum findings necessary for the diagnosis of steatohepatitis includes:

Macrovesicular steatosis, Evidence of hepatocellular injury in the form of hepatocellular ballooning (with or without acidophil bodies or Mallory hyaline) or pericellular Fibrosis. When present along with steatosis, pericellular fibrosis provides evidence of prior steatohepatic injury and is sufficient for the diagnosis even in the absence of hepatocellular ballooning and inflammation.[30]

Acinar inflammation (often mild and mixed) is required for diagnosis of NASH as recommended by Neuschwander –Tetri B.A et al in the AASLD summary conference on NASH in the year 2003.

A mild increase of iron in hepatocytes (Generally non zonal) or sinusoidal cells has been described in 15-55% of cases of NASH with the hepatocytes showing a mild bluish and granular staining.[53]

HEPATITIS

Acute Viral Hepatitis:

Viral hepatitis may be defined as hepatocyte necrosis and hepatic inflammation resulting from systemic viral infection and leading to a characteristic constellation of clinical and morphologic features.

Gross findings:

The liver may be swollen in acute hepatitis and may be discolored yellow or green due to jaundice in massive hepatic necrosis. The liver is soft and flaccid with a wrinkled capsule.

Microscopic findings:

The morphological patterns of acute hepatitis are classic acute hepatitis with spotty necrosis, acute hepatitis with bridging necrosis, acute hepatitis with panacinar necrosis and acute hepatitis with periportal necrosis.[30]

Hepatocytes may also undergo acidophilic changes, in which the cell` becomes shrunken, angular and hypereosinophilic with a densely staining pyknotic nucleus .Such cells may develop in to acidophilic bodies (apoptotic bodies) or councilman bodies.[40]

The Inflammatory infiltrate in acute hepatitis is primarily mononuclear and is composed of lymphocytes, macrophages, scattered eosinophils and occasional plasma cells and neutrophils.

Kupffer cells may contain yellow brown ceriod pigment, staining with PAS after diastase digestion. They may also contain stainable iron, but this is less common.

Individual causes of viral Hepatitis:

Hepatitis A

Teixeira MR, Abe H and Okuno T et al described two main patterns occurring separately or together. One is the histological picture of perivenular cholestasis with little liver cell damage or inflammation.

The second is hepatitis with periportal necrosis and dense portal infiltrate which includes abundant aggregated plasma cells. Extensive microvesicular fatty change of hepatocytes has been seen in severe acute hepatitis A.[48]

Hepatitis B:

The histological appearances are broadly similar to those of other forms of viral hepatitis. However Lymphocytes and macrophages sometimes lie in close contact with hepatocytes (peripolesis) or even invaginate them deeply (Emperipolesis) Periportal Inflammation tended to more

severe in acute hepatitis B. Liver cells and their nuclei may show a moderate degree of pleomorphism. The presence of ground glass hepatocytes or positive staining of surface material indicates chronic disease.[14]

Hepatitis C:

Two distinguished features have been noted in acute Hepatitis C along with the usual features of any other acute hepatitis. First there may be prominent infiltration of sinusoids and portal areas by lymphocytes, in the absence of severe liver cell damage. Second

Lymphoid Follicles and Bile duct damage may be seen within a few weeks or months of onset of hepatitis.

Hepatitis D:

Sanded hepatocyte nuclei may be seen in Hepatitis B with delta virus infection.

Drug related hepatitis may be indistinguishable from viral hepatitis and must rely heavily on clinicopathologic correlations. Features more common in drug induced than in viral hepatitis include sharply defined perivenular necrosis, granulomas, abundant neutrophils or eosinophils and a poorly developed portal inflammatory reaction.[54]

CHRONIC HEPATITIS:

Chronic hepatitis is defined as liver disease with persistant necroinflammatory activity lasting more than 6 months.

The most common causes of chronic hepatitis are viral, autoimmune and drug induced.

Gross findings:

Liver may appear grossly normal in early stages at chronic hepatitis. In later stages, the hepatic parenchyma is firm because of increased fibrosis. Cirrhosis due to viral hepatitis is generally macronodular.[3]

Microscopic findings :

Regardless of etiology, chronic hepatitis is characterized by a combination of portal inflammation, interface hepatitis, parenchymal inflammation and necrosis and in many cases fibrosis.

PORTAL INFLAMMATION :

In most cases of chronic hepatitis a prominent inflammatory infiltrate consisting of lymphocytes with variable number of plasma cells involve the portal tracts. Scattered macrophages, Neutrophils and eosinophils are typically a minor component of the infiltrate. Lymphoid follicles and germinal centres may be seen. Bile duct reaction may be seen at the periphery of the portal tract.

Interface hepatitis also known as piecemeal necrosis or periportal necrosis is an important feature of chronic hepatitis. The lymphocytes and plasma cells of the inflammatory periportal infiltrate are closely associated with degenerating hepatocytes at the limiting plate.[30]

Hepatocytes, in areas of piece meal necrosis often undergo ballooning degeneration and appear pale and swollen with clumping of cytoplasm. Apoptotic bodies may also be seen in areas of active interface hepatitis. The periportal parenchyma is gradually destroyed and replaced by fibrosis.

Lobular Necroinflammatory activity

Hepatocyte necrosis in chronic hepatitis is variable in severity but usually spotty. Apoptotic hepatocytes (acidophil bodies) are scattered throughout the lobule. Mononuclear inflammatory cells clusters around injured hepatocytes and may obscure focal hepatocyte necrosis. Kupffer cells in these areas of spotty hepatocyte necrosis may contain phagocytosed cellular debris.

Ballooning degeneration may be seen in exacerbation of chronic viral hepatitis and may be associated with zone 3 cholestasis. Regeneration of hepatocytes is recognizable by the formation of liver cell plates that are two cell thick and by formation of regenerating

rosettes.[30]

Fibrosis:

Progressive fibrosis at the limiting plate at the result of continued necroinflammatory activity leads to stellate enlargement of the portal

tract. Portal-portal fibrous septa are the result of linkage of adjacent fibrotic portal tracts. Portal central fibrous bridging can also develop generally from superimposed episodes of severe lobular necroinflammatory activity activity involving zone 3. The end result of bridging fibrosis is cirrhosis which is usually macronodular or mixed micro and macronodular.[44]

Other hepatocyte changes seen in chronic hepatitis include steatosis, iron deposition and oncocyte change.

HISTOPATHOLOGY OF SPECIFIC TYPES OF CHRONIC HEPATITIS:

Chronic Hepatitis:

Hepatitis B core antigen (HBcAg) accumulation in hepatocyte nuclei produces a sanded appearance, but such changes are well made out by special stains. Identification of cytoplasmic Hepatitis B surface antigen may be facilitated by use of the Shikata orceins stain.[44]

Delta virus:

Sanded Hepatocytes nuclei may be seen in Hepatitis B with delta virus infection. Delta antigen may be demonstrated within nuclei of

hepatocytes by immuno histochemical stains. Overall, the histopathology resembles hepatitis B without delta infection, but the necroinflammatory activity is often more severe.

Hepatitis C Virus:

Histologically, Chronic hepatitis caused by Hepatitis C tends to be mild. Characteristic features are portal lymphoid aggregates and Follicles, bile duct infiltration by lymphocytes and steatosis. Dense aggregates of lymphocytes in portal tracts are a distinct feature of hepatitis C. The bile duct injury in Hepatitis C is rarely severe.[44]

The biliary epithelium of affected ducts may be focally disrupted in addition to infiltration by lymphocytes and show reactive changes such as vacuolation of epithelium and nuclear crowding and enlargement. Steatosis seen in Hepatitis C is usually macrovesicular and may be associated with more severe necroinflammatory activity.

Chronic hepatitis is of following histological phenotypes .

1) Minimal hepatitis diagnosed by the constant findings of discrete lymphocytic infiltrate in some portal tracts and scanty intra acinar lymphocytic foci.

2) Chronic persistant hepatitis diagnosed by the constant findings of intact limiting plate, chronic inflammation of portal tracts with lymphocyte predominance and slight focal intra acinar inflammation.

3) Chronic lobular hepatitis diagnosed by the constant findings of pronounced spotty necrotic hepatitis, portal lymphocytic inflammation and preserved acinar architecture.

4) Chronic active hepatitis diagnosed by the constant findings of portal and periportal lymphocytic inflammation, periportal piecemeal necrosis, focal intra acinar inflammation and portal tracts with a maple leaf configuration.[30]

CIRRHOSIS

Cirrhosis is a neologism coined by Laennec, meaning tawny.

Cirrhosis is a diffuse process in which the normal lobules are replaced by architecturally abnormal nodules separated by fibrous tissue.[4]

Cirrhosis represents end stage chronic liver disease and is associated with variety of etiologies .The most common causes of cirrhosis are alcoholic liver disease followed by chronic viral hepatitis, autoimmune hepatitis, primary sclerosing cholangitis , primary biliary cirrhosis and metabolic disorders .

Macroscopic appearance:

Micronodular cirrhosis:

The overall shape and external appearance of the liver in micronodular cirrhosis may not be greatly altered.The nodules on the cut surface are small in size and uniform in appearance but may be difficult to define.

The nodules are less than 3 mm in diameter. The ratio of fibrous matrix to parenchyma is greater than in macronodular and consequently the liver is firm or even hard. Fibrosis is diffusely distributed as fine, indistinct bands between nodules but occasionally these may be broader and define more clearly the nodules on both the cut and capsular surfaces. In the early stages, the liver may be enlarged but with advancing disease, it shrinks in size. Alcohol is most frequently associated with micronodular pattern.[30]

Alcoholic liver disease shows a diffuse tan or yellow color due to severe fatty changes.

Macronodular cirrhosis:

The size of the liver in macronodular cirrhosis is much more variable .It is frequently enlarged but, when associated clinically with liver failure, is usually small and may weigh less than 1000 g. The parenchyma is organized in large bulging nodules which are separated by fibrous bands that vary considerably in width.

In the early stage, slender fibrous bands are seen , but as the disease progresses , these become broader and denser and produce marked grooving and retraction which is visible on capsular surface .This is the pattern of cirrhosis mast frequently seen at autopsy as it represents the end stage of almost any form of chronic liver disease.[30]

Incomplete septal Cirrhosis:

Macronodular cirrhosis of an incomplete septal pattern is characterized by ill.defined large bulging nodules with only slender fibrous septa and microscopic examination may be required for its identification. It is most frequently seen in chronic hepatitis B virus infection.

Microscopic features:

Normal acini are approximately 1mm in diameter and consequently 3 mm nodules in micronodular cirrhotic liver may contain complete acinar units within them. More commonly, the acini are subdivided into nodules, creating a micro micro-nodular pattern and virtually every acinus is involved. This micro, micronodular pattern is most commonly associated with alcohol and metabolic disturbances like haemochromatosis.

Fibrosis is seen in zone 1, 2 &3 and the fibrovascular septa transects the acinus before

abnormal nodules are formed in typical alcoholic liver disease. The fibrosis is focused around the terminal hepatic venules and extends through the sinusoids towards the portal tracts with subacinar areas of parenchyma isolated by these irregular fibrous bridges.[30]

All the major hepatic vascular structures are peripheral to the small nodules so that abnormal patterns of flow are created through the

nodule. Gradually these foci link to produce a more diffuse network of fibrosis and eventually cirrhosis.

The tiny nodules enlarge as they regenerate, become rounded and develop a pseudocapsule by compression of surrounding connective tissue. Such regenerative nodules can be larger than a simple acinus but less than 3 mm in diameter and lack any acinar substructure. If their expansile growth continues, the nodules become larger than 3 mm in diameter and evolution into macronodular cirrhosis occurs.

MACRONODULAR CIRRHOSIS:

Histologically 3 patterns can be identified these are incomplete septal , multiacinar and regenerative.[30]

INCOMPLETE SEPTAL CIRRHOSIS:

It has a pattern characterized by very slender fibrovascular septa that extends from portal tracts into the parenchyma but often do not interconnect with other portal tracts or hepatic veins. There is little evidence of cell damage or death and little or no inflammation is seen in the septa. Abnormal architectural patterns are present and can be identified as a variable mixture of twinned cell plates and dilated sinusoids.

Multiacinar macronodular cirrhosis:

It probably represents an early stage of evolution. The large nodules are defined by abnormal septa but within them some residue of the original architecture can still be maintained which may be represented by one or more minimally distorted portal tracts within the nodule.[30]

Regenerative macronodular cirrhosis:

The nodules are rounded, large and tumor like. Regenerative activity like twinning of cell plates and increased nuclear pleomorphism of hepatocytes is more obvious.

Architectural changes are best appreciated on a reticulin stain. The size of the nodules is relative as in most cases the micronodular one eventually transforms in to macronodular type. Most important is to comment on the etiology of cirrhosis like presence of interface hepatitis in post necrotic cirrhosis, presence of steatohepatitis in chronic alcoholism and NASH and ductopenia in primary biliary cirrhosis.[25]

Bartok I, Remenar E et al studied about demonstration of hepatitis B surface antigen by Orcein staining in paraffin sections of cirrhotic liver and found it useful as a simple handy procedure for detecting HBSAg in stored paraffin blocks.[7]

LIVER CELL DYSPLASIA:

Liver cell dysplasia was first described by Anthony et al who proposed strict morphological criteria for its identification. Apart from its frequent association with hepatocellular carcinoma, it is also frequently found in association with chronic hepatitis B virus infection.[5] Two morphological types namely large cell dysplasia and small cell dysplasia has been described and the general criteria proposed by Anthony et al are cellular enlargement, nuclear pleomorphism with hyperchromasia and multinucleation, in groups of liver cells, or occupying whole cirrhotic nodules and nuclear:cytoplasmic ratio being normal in large cell dysplasia and increased in small cell dysplasia.[5]

The presence of dysplasia in the non tumor portion of hepatocellular carcinoma points towards a viral etiology and its presence in normal liver points towards a premalignant process.

Anthony et al studied the incidence of large cell dysplasia in a large group of patients from Uganda and found it in only 1% of patients with normal liver, in 6.9% of patients with liver cell carcinoma occurring in a otherwise normal liver, in 20.3% of patients with cirrhosis and in 64.5% of patients with cirrhosis and liver cell carcinoma.[5]

Lefkowitch J H, Apfelbaum et al showed the presence of dysplastic changes in cases of viral hepatitis.[27]

METASTASES :

Liver is a common site for metastases particularly from carcinomas of lung, breast(Fig 5,6) and gastrointestinal tract. Points in favour of a primary tumor are a diffuse infiltrative growth pattern and also intrabiliary spread.[15]

Borja E R, Hori et al reported 25 cases of carcinomatous cirrhosis with jaundice, ascites

and bleeding esophageal varices, most of them due to diffuse infiltration of liver by metastatic breast carcinoma.[9]

Gerber et al described characteristic histological triad in liver adjacent to metastatic neoplasm comprising of proliferating bile ducts, presence of leukocytes and presence of focal sinusoidal dilatation.[21]

The primary site mostly cannot be identified histopathologically and use of immunohistochemical analysis is needed. The mesenchymal tumors which may metastasize to liver are leiomyosarcoma and gastrointestinal stromal tumors.

MATERIALS and METHODS

MATERIALS AND METHODS

The core material forming the basis of this study comprised of 100 specimens of liver obtained from post mortem examinations done in the Forensic medicine department of Madras Medical College Chennai. The study was a prospective one done during a period of six months from consecutive autopsies during a span of January 2007 to July 2007.

Post mortems done in our institutions are usually cases of road / railway accidents, poisoning and fall.

All livers were examined carefully for gross abnormalities and weight measured for all livers. Specimens were fixed in 10% formalin and random bits taken from each specimen, 2 bits from right lobe and 2 bits from left lobe. Histologic sections (5 to 6 um) were routinely stained with hematoxylin and eosin stains. Special stains like PAS, RETICULIN, PERLS', and ORCEIN were done for all the cases.

PROCEDURES

II. PAS TECHNIQUE (MC MANUS)

1. Dewax sections and bring to distilled water.
2. Treat with per-iodic acid for 5 minutes.
3. Wash well with several changes of water.
4. Cover with Schiffs solution for 15 minutes.

5. Wash in running tap water for 5–10 minutes .
6. Stain nuclei in Harris Hematoxylin differentiating as appropriate in acid alcohol and blueing as usual.
7. Wash in water.
8. Rinse in absolute alcohol.
9. Clear in xylene and mount.

RESULTS

Glycogen in cytoplasm of hepatocytes = magenta

Nuclei = blue.

III. **GOMORIS METHOD FOR RETICULAR FIBRES**

1. After Dewaxing, bring sections to water.
2. Treat with 1% potassium permanganate solution for 2 minutes.
3. Rinse in tap water.
4. Bleach in 2 % potassium metabisulfate solution.
5. Rinse in tap water.
6. Treat with 2 % iron alum for 2 minutes.
7. Wash in several changes of distilled water.
8. Place in coplin jar of silver solution 1 minute.
9. Wash in several changes of distilled water.

10. Reduce in 4% aqueous formalin solution, 3 minutes.
11. Rinse in tap water.
12. Tone in 0.2 % gold chloride solution, 10 minutes.
13. Rinse in tap water.
14. Treat with 2% potassium metabisulfite solution for 1 minute.
15. Rinse in tap water.
16. Treat with 2 % sodium thio sulfate solution, 1 minute.
17. Rinse in tap water.
18. Dehydrate through alcohols.
19. Clear in xylene and mount.

INFERENCE

Reticular Fibres= Black.

PERLS' STAIN

PROCEDURE:

1. DPHW.
2. Place slides in a equal volume of aqueous solutions of 2% aqueous potassium ferrocyanide and 2% hydrochloric acid for 10 minutes at room temperature.
3. Rinse in distilled water.
4. Counterstain in 0.1 % nuclear fast red solution for 5 minutes.

5. Wash thoroughly in running tap water for 2 minutes.
6. DHCM.

RESULTS:

Hemosiderin and some oxides and salts of iron =blue

Nuclei and cytoplasm = pink to red.

MODIFIED SHIKATAS ORCEIN STAIN

Shikatas orcein solution is prepared by dissolving 1 g of orcein powder in 100 ml of 70 % alcohol. Add 1 ml of concentrated nitric acid. Leave this solution at room temperature for 24 hrs before use. The solution is then kept in the refrigerator and is good for 3 months.

PROCEDURE:

1. DPHW.
2. Oxidize in freshly prepared acidified potassium permanganate for 5 minutes.
3. Bleach in 2 % aqueous solution of oxalic acid for 1 minute or until the sections turn white.
4. Wash well in water.
5. Rinse briefly in 70 % alcohol.
6. Place in modified Shikatas solution for 10 minutes.
7. Remove excess stain in 70 % alcohol.

8. DHCM.

RESULTS:

Hepatitis B surface antigen, elastic fibers. = **DARK BROWN**

MICROSCOPIC FEATURES:

Histomorphological criteria for each of the histological entities were as follows.

Steatosis (Fig.7) diagnosed by the presence of fatty change and graded as 1+ to 4+ depending on the percentage of liver cells containing fat.[42]

Steatohepatitis (Fig.8) diagnosed by the presence of pericellular fibrosis, portal and acinar inflammation, Ballooning degeneration, hepatocyte necrosis in addition to fatty change.[10]

Chronic venous congestion(Fig.9) diagnosed by the presence of sinusoidal dilatation, congestion and presence or absence of centrilobular necrosis.

Chronic hepatitis diagnosed by the minimal criteria like interface hepatitis, portal inflammation and spotty necrosis.(Fig.12&18)[30]

Cirrhosis(Fig.10) diagnosed by the presence of regenerative nodules and fibrosis.

Liver cell dysplasia(Fig.16) diagnosed by the presence of cellular enlargement, nuclear pleomorphism, multinucleation but with normal nuclear: cytoplasmic ratio.[5]

Ground glass hepatocytes stained positive for Orcein were graded using the following criteria.

Type I showing a positive staining of cytoplasmic periphery (marginal GGH), Type II showing a diffuse staining(Diffuse GGH), Type III showing globular positive cytoplasmic masses (Globular GGH), Type IV showing spotty drop like positive structures and Type V featuring positive staining ground glass hepatocytes with fatty changes .[8]

DISCUSSION

DISCUSSION

This study deals with the histomorphological characteristics of the liver specimen obtained in the age grou
20 - 80 years in 100 consecutive medico-legal autopsy cases. The causes of deaths were due to road / rail
accidents, poisoning, burns and hanging. No medical history was available in any of these cases. The l
tissue obtained were processed as described earlier and screened for various morphological parameters suc
fatty change, necrosis, fibrosis, cirrhosis etc.

Out of the 100 cases, 49 showed a normal histology. Rest of the cases showed various morphological feat
which are shown in the chart No.1. Fatty change was the most predominant finding accounting to 25% (n=
with steatosis in 17 cases (17%) and 8 cases (8%) showing accompanying hepatitis component. Chr
venous congestion was the next common morphological finding which was seen in 12 cases (12%).

Six cases (6%) showed features of chronic hepatitis, 4 cases (4%) of cirrhosis and 2 cases of each metast
and liver cell dysplasia (2% each) were seen.

Each of the morphological features were analysed with respect to various parameters such as age, sex, weight of the liver and relations to special stains and the observations discussed here under.

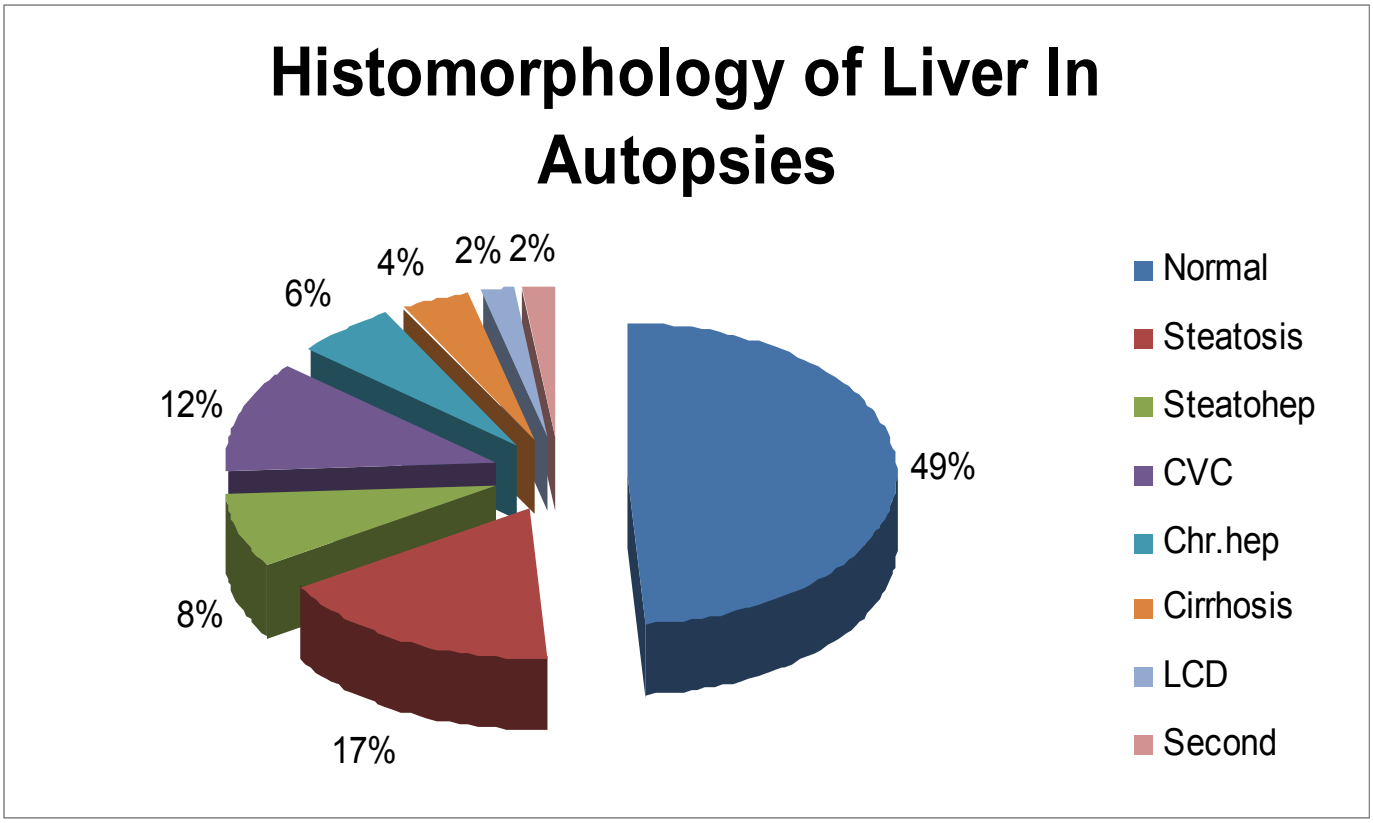


CHART 1

The cases were sub grouped as follows keeping age as denominator.

Group A: (21-30)

Group B: (31-40)

Group C: (41-50)

Group D: (51-60)

Group E: (61-70)

Group F: (71-80)

Table 1. Steatosis -Age & Sex distribution

Age	Male	Female	Total	Percentage
21-30 yrs	2	0	2	11.8%
31-40yrs	6	1	7	41.10%
41-50yrs	1	1	2	11.80%
51-60yrs	6	0	6	35.30%
61-70yrs	0	0	0	0%
71-80yrs	0	0	0	0%
Total	15	2	17	100%

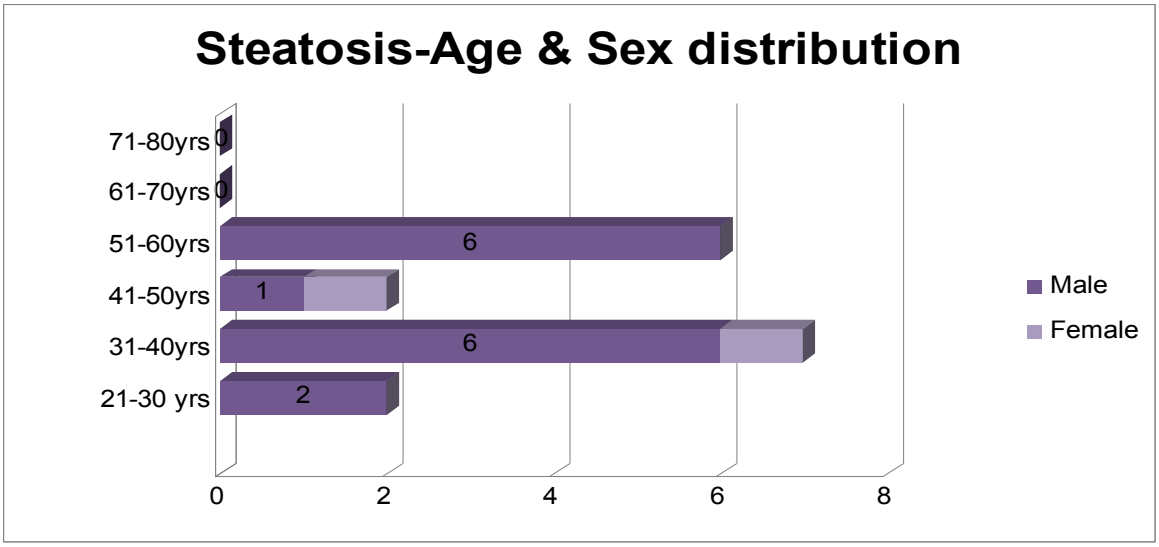


CHART 2

GROUP A:

Of 14 cases in the age group of 21-30 years, 12 were males and 2 were females. 2 cases showed features of steatosis (14.3%), both males and the remaining 12 cases (85.7%) were of normal histology.

PAS and Iron stain did not show any significant features in this group. However, Orcein stain showed positivity in 3 cases in this group, 2 normal cases and one case of steatosis. All the three were males accounting to 21.4% in this group.

Group B:

In the age group of 31-40 years, 18 were males and 6 were females. Ten of these cases showed normal histology (41.6%). Of the rest seven cases showed steatosis (29.2%), of which 6 cases were male and one was a

female, 3 cases showed chronic venous congestion (12.5%) with 2 males and one female, 3 (12.5%) steatohepatitis with two males and one female. One (4.2%) had features of chronic

hepatitis which was a female.

PAS and Iron stain did not show any remarkable features. Reticulin stain highlighted the bridging fibrosis, pericellular fibrosis and perivenular fibrosis in cases of steatohepatitis and chronic hepatitis.(Fig 13)

Orcein staining showed positivity in 2 cases accounting to 8.3% in this group. Both the cases were males showing features of steatosis.

Table 2. STEATOHEPATITIS Age & Sex distribution

Age	Male	Female	Total	Percentage
21-30 yrs	0	0	0	0
31-40yrs	2	1	3	37.50%
41-50yrs	2	1	3	37.50%
51-60yrs	0	1	1	12.50%
61-70yrs	1	0	1	12.50%
71-80yrs	0	0	0	0
Total	5	3	8	100

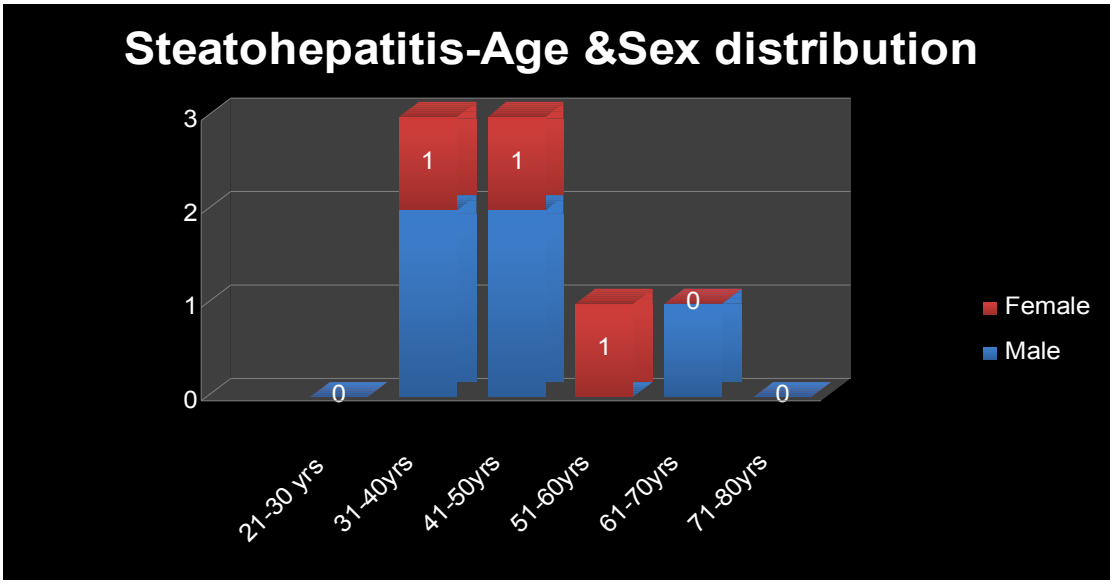


CHART 3

Group C:

In this group of 41-50 years, which had 26 cases 20 were males and 6 were females. In this group 2 cases each of male and female showed steatosis (7.7%), five all males showed chronic venous congestion (19.2%), 3 showed features of steatohepatitis of which 2 were males and one was a female (11.5%), 4 cases showed chronic hepatitis (15.4%) 2 of each male and female, 1 case of male showing cirrhosis (3.8%), and one female with metastatic disease (3.8%) the rest showed normal histology (38.6%).

PAS and Iron stain did not show any remarkable features in this group.

Reticulin stain highlighted the features of cirrhosis, chronic hepatitis and steatohepatitis.

Orcein stain showed positivity in 5 cases (3 male and 2 females) accounting to 19.2%, of which 2 were morphologically normal, one case was chronic hepatitis,1 case of cirrhosis and of one of steatosis.

Positivity for orcein in a case of chronic hepatitis probably implicated the etiology to be hepatitis B.(Fig 21)

Table 3. Chronic Venous Congestion of Liver –Age &Sex distribution

Age	Male	Female	Total	% of Age
21-30 yrs	0	0	0	0
31-40yrs	2	1	3	25%
41-50yrs	5	0	5	41.7%
51-60yrs	1	1	2	16.7%
61-70yrs	1	0	1	8.3%
71-80yrs	1	0	1	8.3%
Total	10	2	12	100%

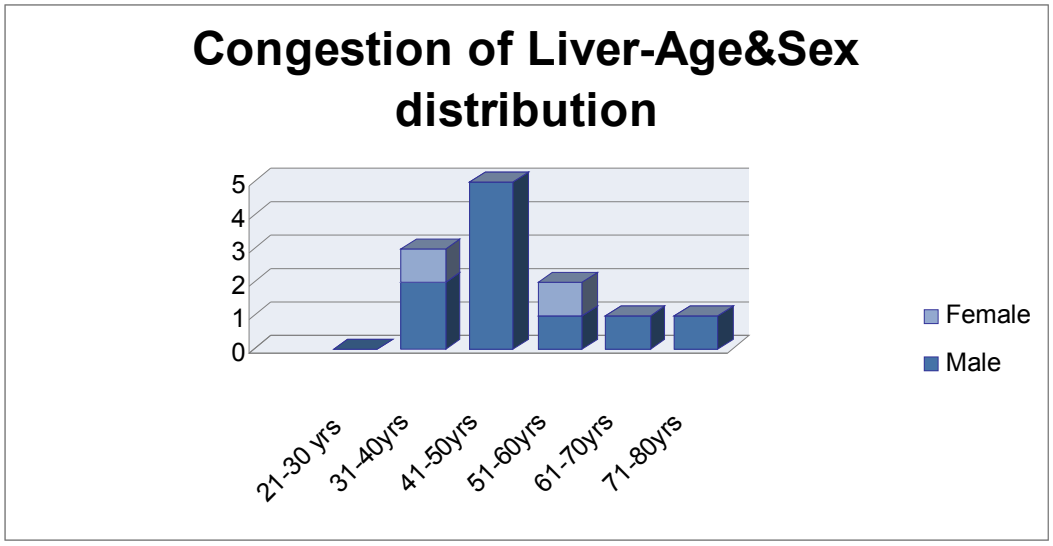


CHART 4

GroupD:

In the group of 51-60 years forming a total of 24 cases, 18 were males and 6 were females. Six males showed steatosis (25%), one each of male and female showed chronic venous congestion (8.2%), one female showed steato-hepatitis (4.2%) and one male showed chronic

hepatitis (4.2%) and a male with metastatic disease (4.2%) and the rest were normal (54.2%). PAS and iron stain did not show any significant features.

Reticulin stain was significantly helpful to highlight a case of chronic hepatitis in a male which was not identified by routine hematoxylin and eosin staining.(Fig 13)

Orcein staining showed positivity in 2 cases, one male and one female accounting to 8.3% in this group. Both of these cases had only steatosis.

Table 4. Cirrhosis-Age&Sex distribution

cirhosis	Male	FEMALE	TOTAL	% of Age
21-30 yrs	0	0	0	0%
31-40yrs	0	0	0	0%
41-50yrs	1	0	1	25%
51-60yrs	0	0	0	0%
61-70yrs	3	0	3	75%
71-80yrs	0	0	0	0%
TOTAL	4	0	4	100%

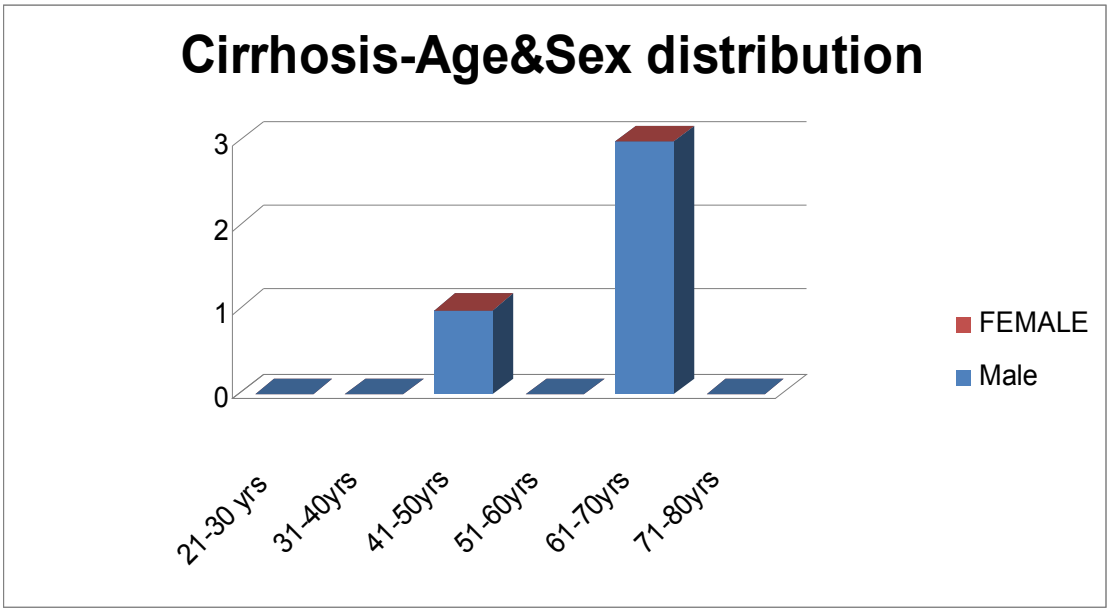


CHART 5

Table 5. CHRONIC HEPATITIS Age & Sex distribution

Age	Male	Female	Total	% of Age
21-30 yrs	0	0	0	0%
31-40yrs	0	1	1	16.70%
41-50yrs	2	2	4	66.60%
51-60yrs	1	0	1	16.70%
61-70yrs	0	0	0	0%
71-80yrs	0	0	0	0%
Total	3	3	6	100%

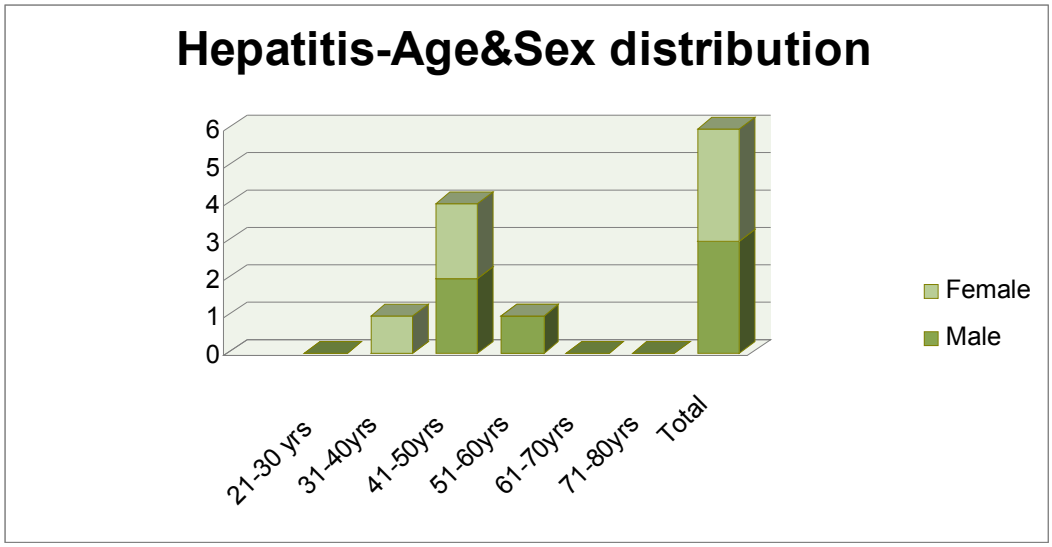


CHART 6

Table 6. LCD Age&Sex distribution

Age	Male	Female	Total	% of Age
21-30 yrs	0	0	0	0%
31-40yrs	0	0	0	0%
41-50yrs	0	0	0	0%
51-60yrs	0	0	0	0%
61-70yrs	0	0	0	0%
71-80yrs	1	1	2	100%
Total	1	1	2	100%

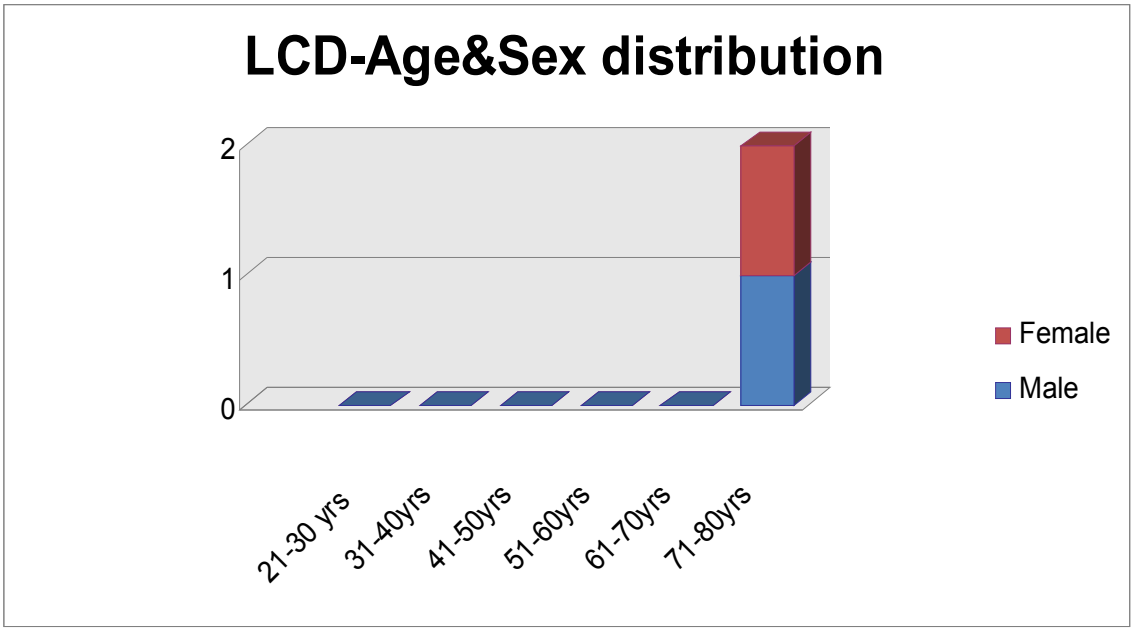


CHART 7

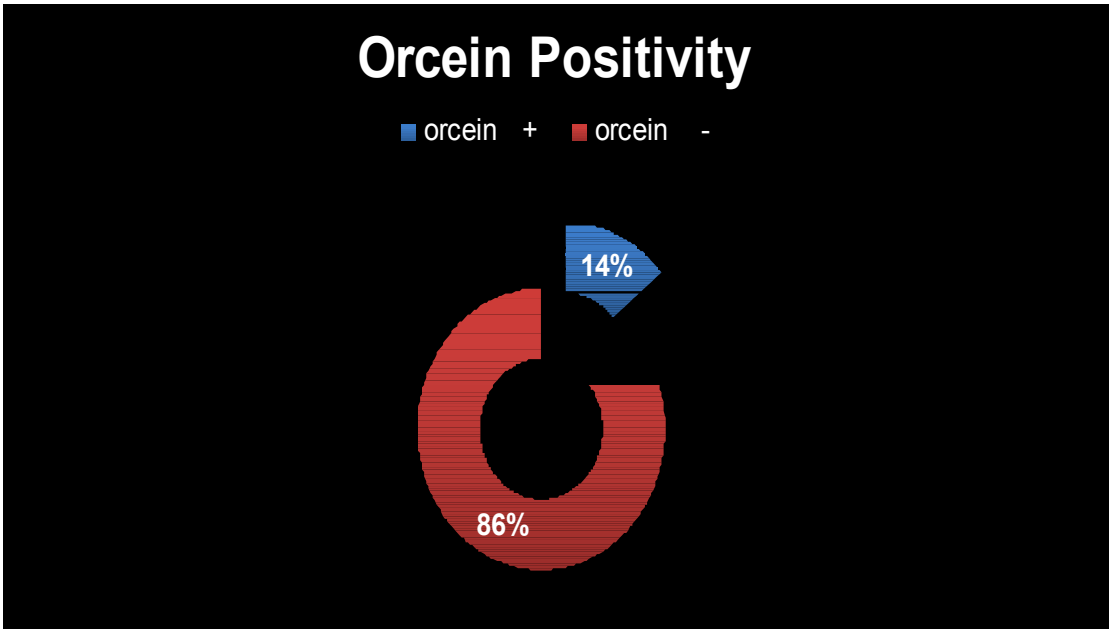


CHART 8

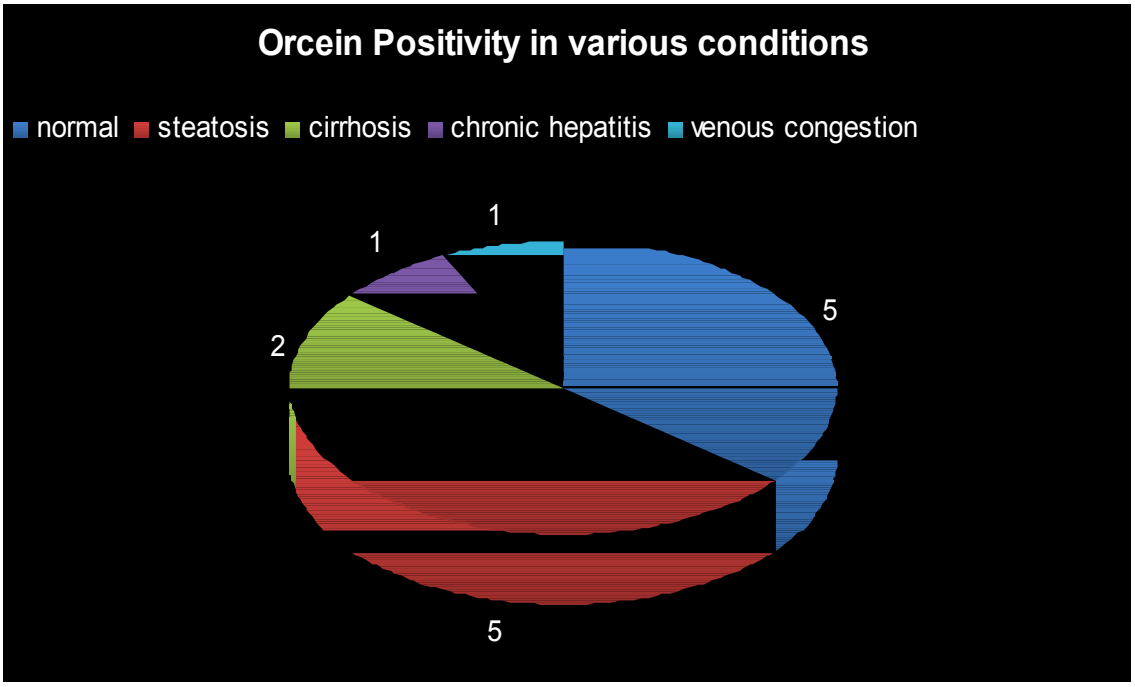


CHART 9

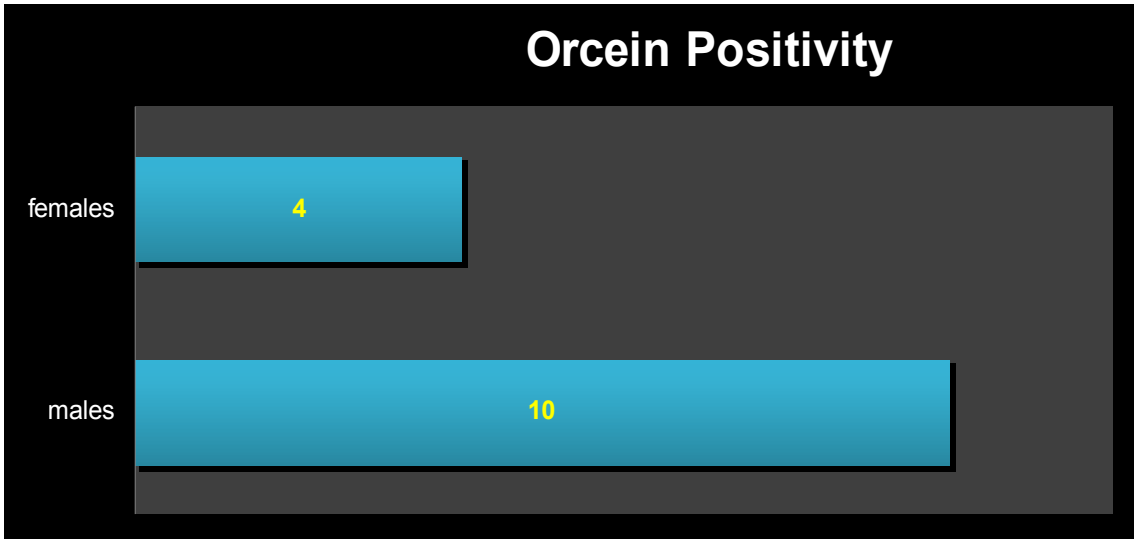


CHART 10

Group E:

In the age group of 61-70 years, from a total of 8 cases, all males three showed cirrhosis (37.5%) one steatohepatitis (12.5%) and one chronic venous congestion (12.5%) and three (37.5%) had normal histology.

PAS stain did not show any remarkable features.

Iron stain showed increased iron stores (grade of 2+positivity) in a case of micronodular cirrhosis probably suggesting alcohol as etiological factor. Of the three cases of cirrhosis, one showed orcein positivity probably indicating viral etiology.

Reticulin stain highlighted the nodules in cirrhosis.(Fig 11)

Orcein stain showed positivity in one case of cirrhosis accounting to 12.5 % in this group.

Group F:

In this group of 71-80 years comprising of four cases, two were males and two were females. One male showed chronic venous congestion (25%), one each of male and female showed features of Liver cell dysplasia (50%) and one female showed normal histology (25%)

PAS and iron stain did not show any remarkable features in this group.

Orcein stain showed positivity in one female with normal histology accounting to 25% in this group.

Steatosis was the most predominant histological abnormality seen in 17% of all cases in the study. It was dominating in the 4th decade accounting to 41.1% and falling to 35.3% in the 6th decade. Males were the most affected gender.(table 1). This finding compared well with study of **M.S.Bal, S.P.Singh** et al,[6] with steatosis was seen in 53.85% in 5th decade falling to 35.99% in 6th decade in their study which included cases > 40 years of age and

Sotoudehmanesh, Sotoudeh et al, steatosis was noted in 31.6%.in a study of 896 autopsies.[46] However, a study by Ghazala Anif, Hannan et al on incidental findings in 110 liver autopsies fatty change was noted in only 4.5% of cases.[22]

Among the cases with fatty change, 8 cases showed features of hepatitis in addition to steatosis and were categorized as cases of steatohepatitis.

Steatohepatitis was mostly seen in 4th and 5th decade comprising about 37.5% in each decade with males predominating the picture (table 2) The females cases in this group probably representing nonalcoholic steatohepatitis, which is beginning to emerge as one of the most common liver disorders occurring in non–alcoholics. The study of Sotoudehmanesh, Sotoudeh et al, wherein steatohepatitis was seen in 2.1% compared well with our observation though on lower proportion which may be because of

social and racial differences.-[46] however the study of Bal et al. did not report any in their study.

Chronic Venous Congestion of liver was the next common abnormality closely following fatty change in our study accounting to 12 cases.(Fig 9) The majority of cases were in 5th decade accounting to 41.7% in this category. Out of total 12 cases, 10 were males and 2 were females (Table 3). Bal et al reported a higher percentage 77.8% in the 5th decade. Copelands (1985) study reported congestion with fatty change in 3.4% of liver autopsies of alcoholics[6] and Ghazala Anif, Hannan et al (2001) reported venous congestion in 2.7%.

Cirrhosis liver was seen in 4 cases (4%) in our study. Grossly, two were micronodular,(Fig 1,2) one macronodular and one was mixed in type. All the four cases were males and

constituting about three cases (75%) in the 61-70 years group and one (25%) in 41-50 years group (Table 4). Bal et al reported 14 cases of cirrhosis with 42.85% in 41-50 years group, Ghazala, Hannan et al reported cirrhosis in 4.5% and Sotoudehmanesh, Sotoudeh et al, reported cirrhosis in only 0.8%.[46]

Chronic hepatitis was seen in 6 cases (6%) in total. The major bulk was seen in 41-50 years group accounting to 66.6% .The male:female ratio was equal, each constituting about 3 cases (Table 5).

Bal et al, reported 3 % cases of hepatitis, Sotoudehmanesh, Sotoudeh et al, reported chronic hepatitis in 2.6% and Ghazala Anif Hannan et al, reported in chronic hepatitis in 12.7%.[46]

Liver cell dysplasia was seen in 2 cases, both in age group of 71-80 years with one male and one female.(Fig 16). None of the referred studies reported cases of liver cell dysplasia. However, Anthony et al (1973) reported about 1% in normal liver.

Orcein staining was done in all 100 cases to assess generalized and random prevalence of Hepatitis B surface antigen. 14 cases showed positivity for Orcein.(chart 8). Of the 14 cases, five of the cases showed normal histology, five with steatosis, two with cirrhosis, one each of chronic hepatitis and chronic venous congestion (chart 9).

The typing of staining was carried out according to the typing proposed by Borchard and Gussman (1979).[8]

Of the five cases with normal histology four showed type I and one type II.(Fig 21). Three of five cases of steatosis showed type I and two type II.

CVC showed type I positivity.

In cases of cirrhosis one showed type II and one type III was seen.

In case of chronic hepatitis type III was observed.

Type I and II staining signify in all carriers and minimal hepatitis.(Fig 22).

Type II and type III staining pattern was observed in chronic persistent hepatitis.

PAS staining was done to assess glycogenation but did not reveal any significant features.

Perl s' staining was done to assess iron stores in varied liver diseases and to pick up cases of hemochromatosis in a random manner. A case of cirrhosis showed increased iron stores (grade of 2+) but the other cases did not show any increased iron stores.

FIG 1- GROSS CIRRHOSIS LIVER - EXTERNAL APPEARANCE

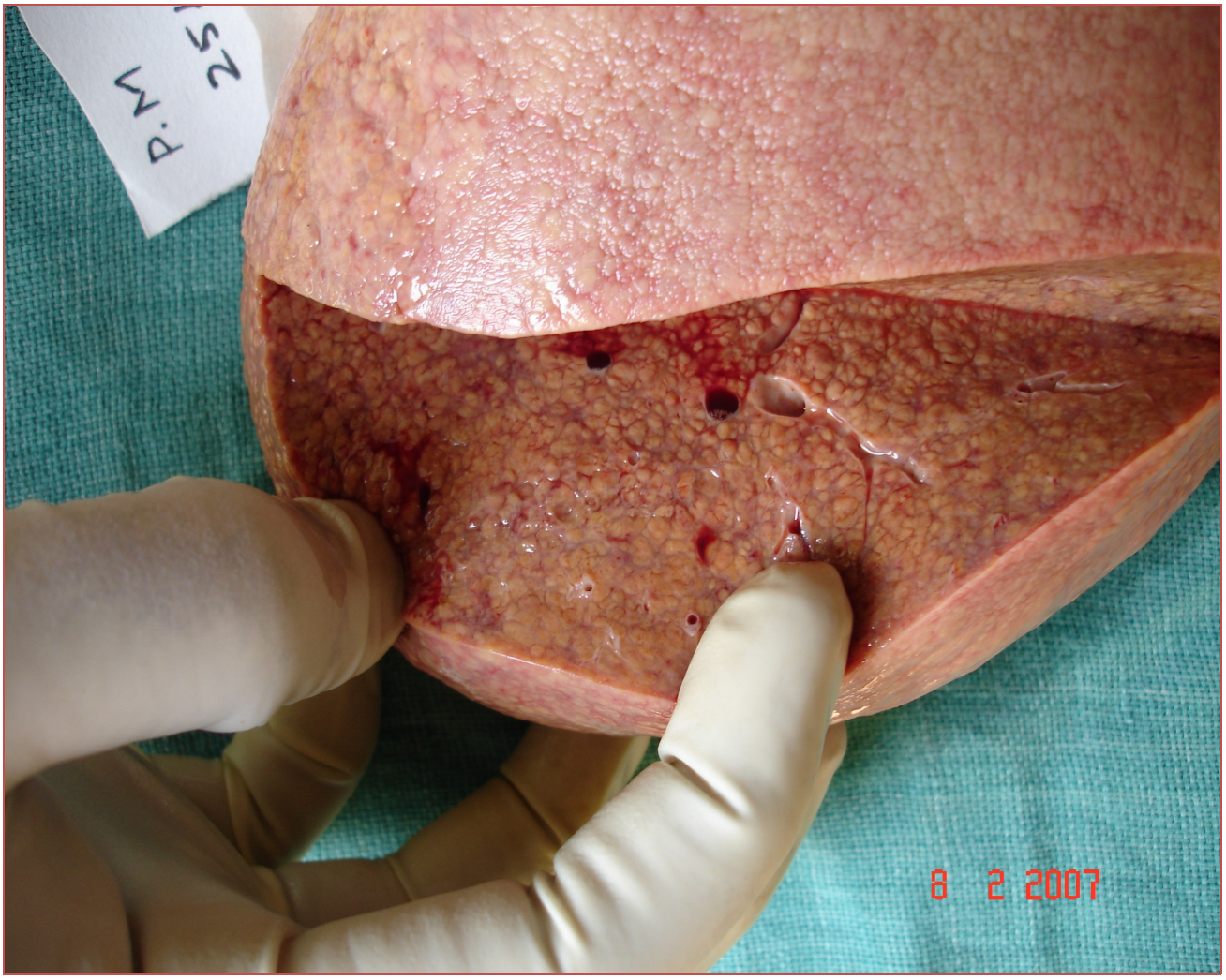


FIG 2 – GROSS CIRRHOTIC NODULES CUT SURFACE

Fig 3 – congestion liver – cut surface

Fig 4 – fatty liver – cut surface

Fig 5 – metastatic deposit- cut surface

Fig 6 – metastatic deposit – external surface

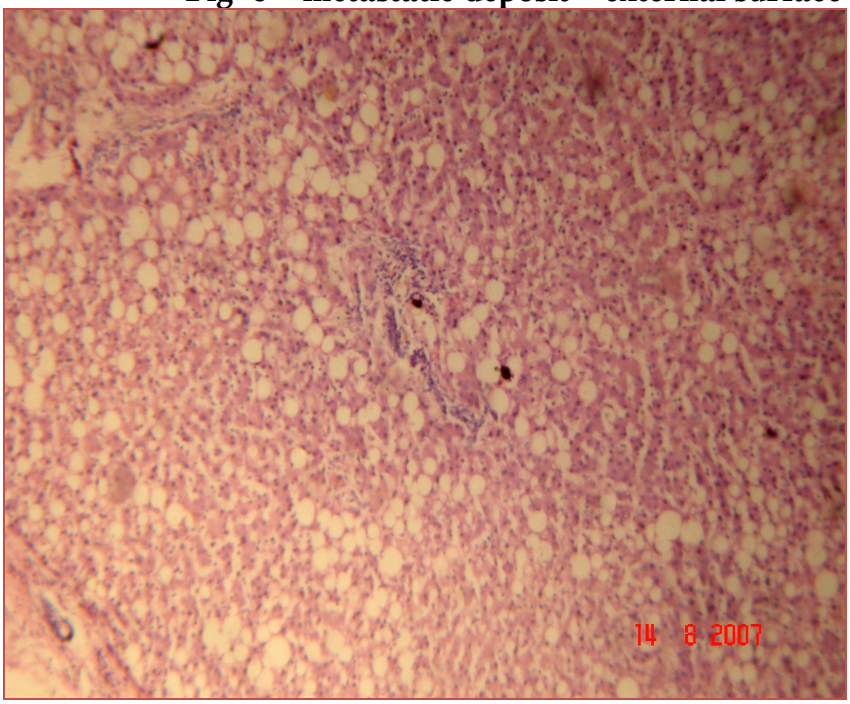


Fig 7 - steatosis – low power (100x)

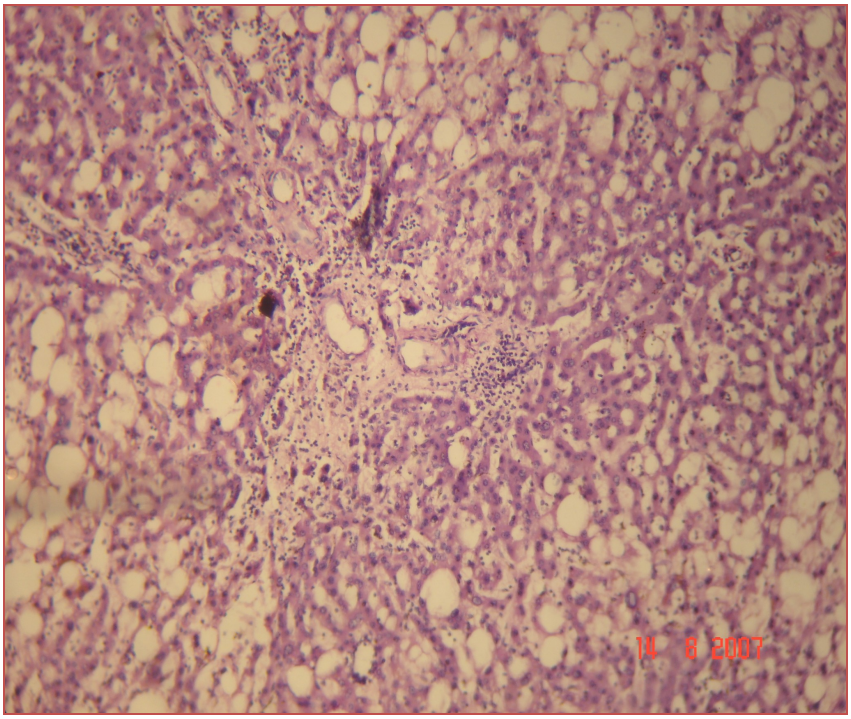


Fig 8 – steatohepatitis – low power (100x)

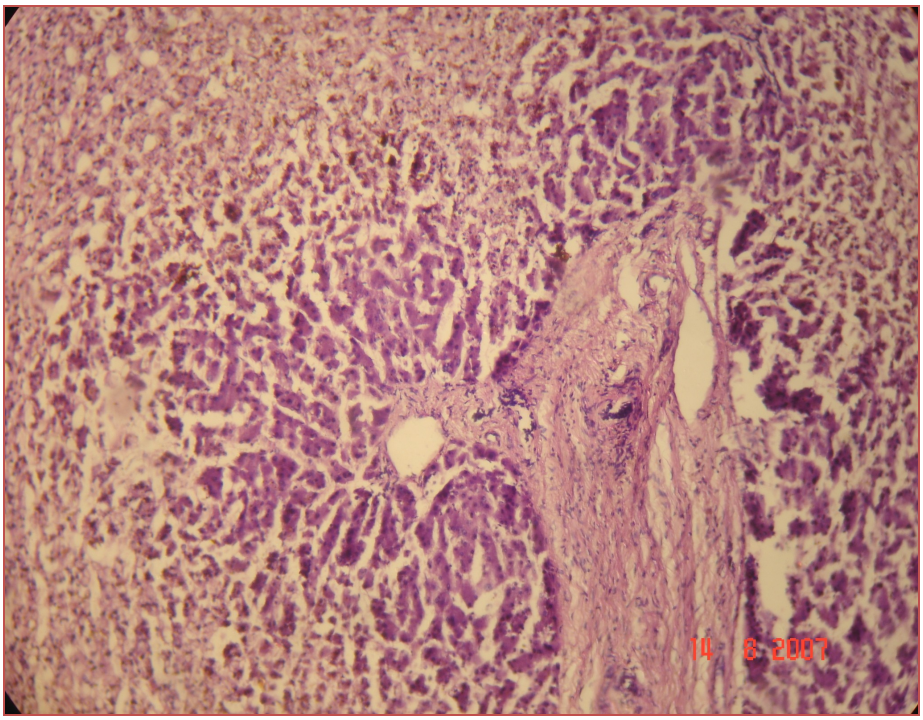


Fig 9 – chronic venous congestion liver –
viable periportal hepatocytes-low power

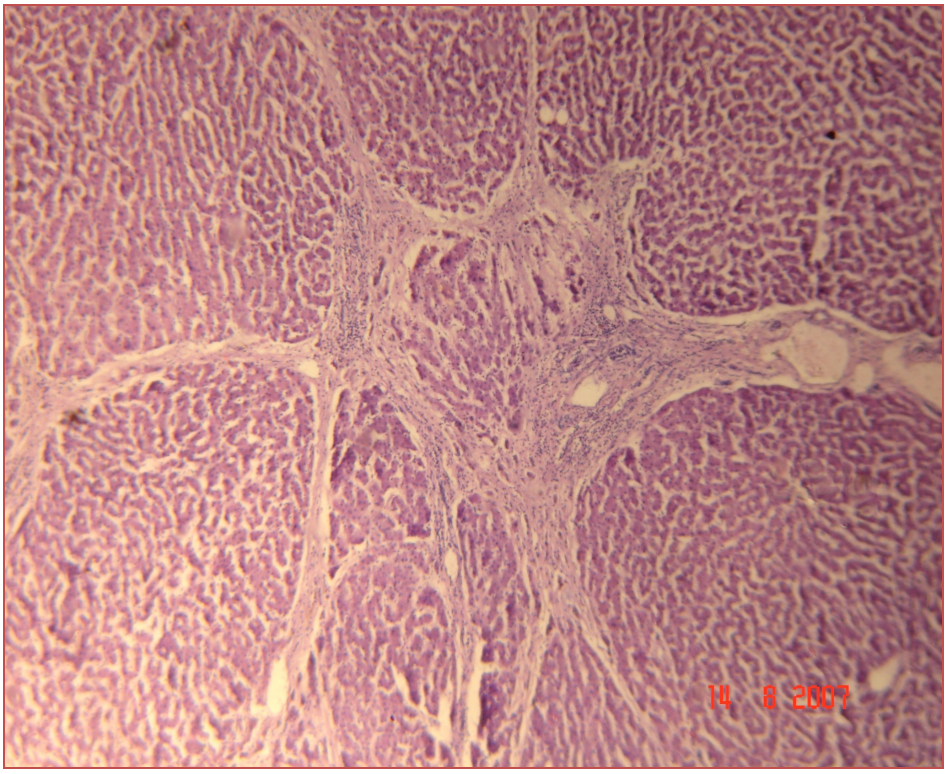
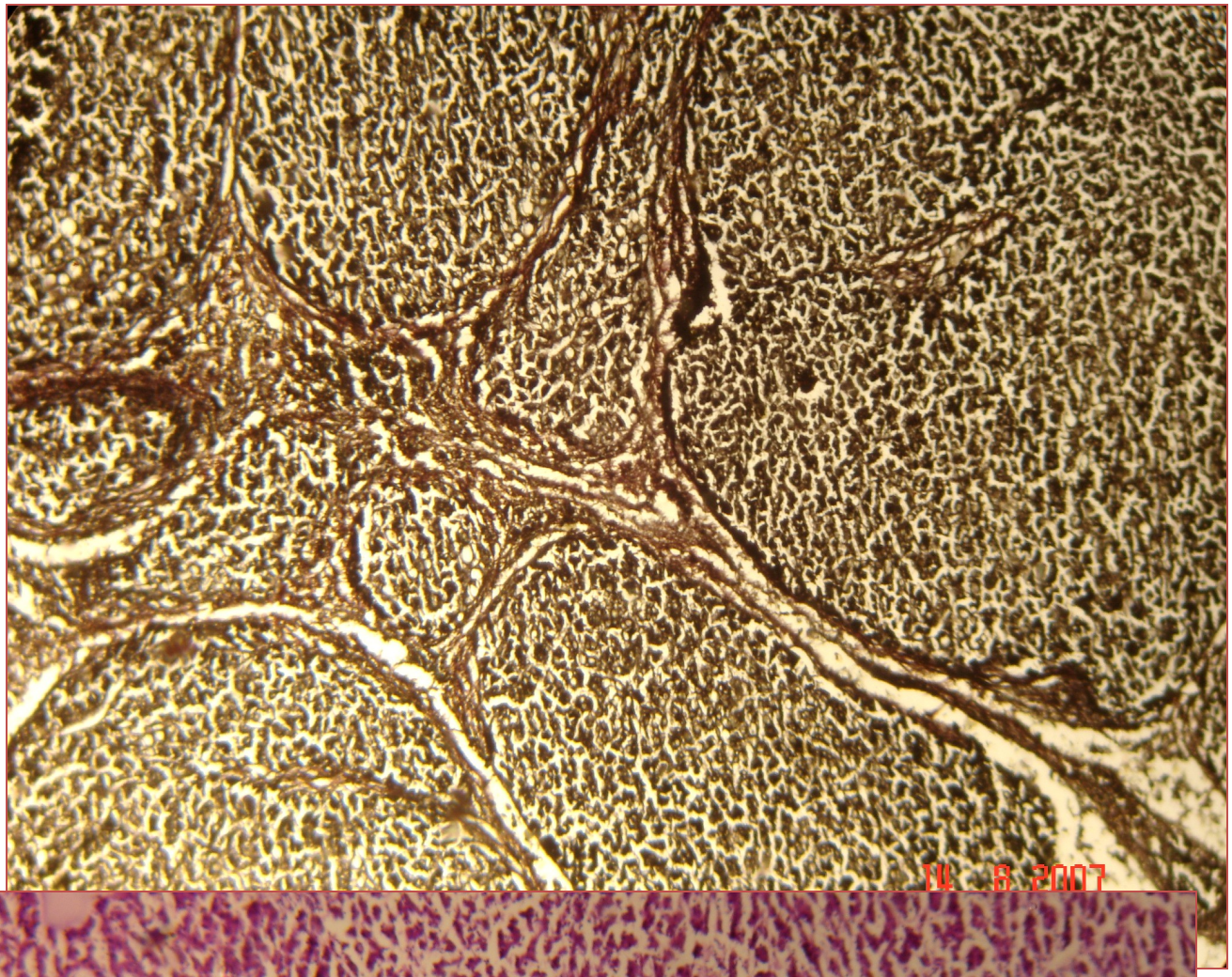


Fig 10 – cirrhosis lowpower (100x)


14 8 2007

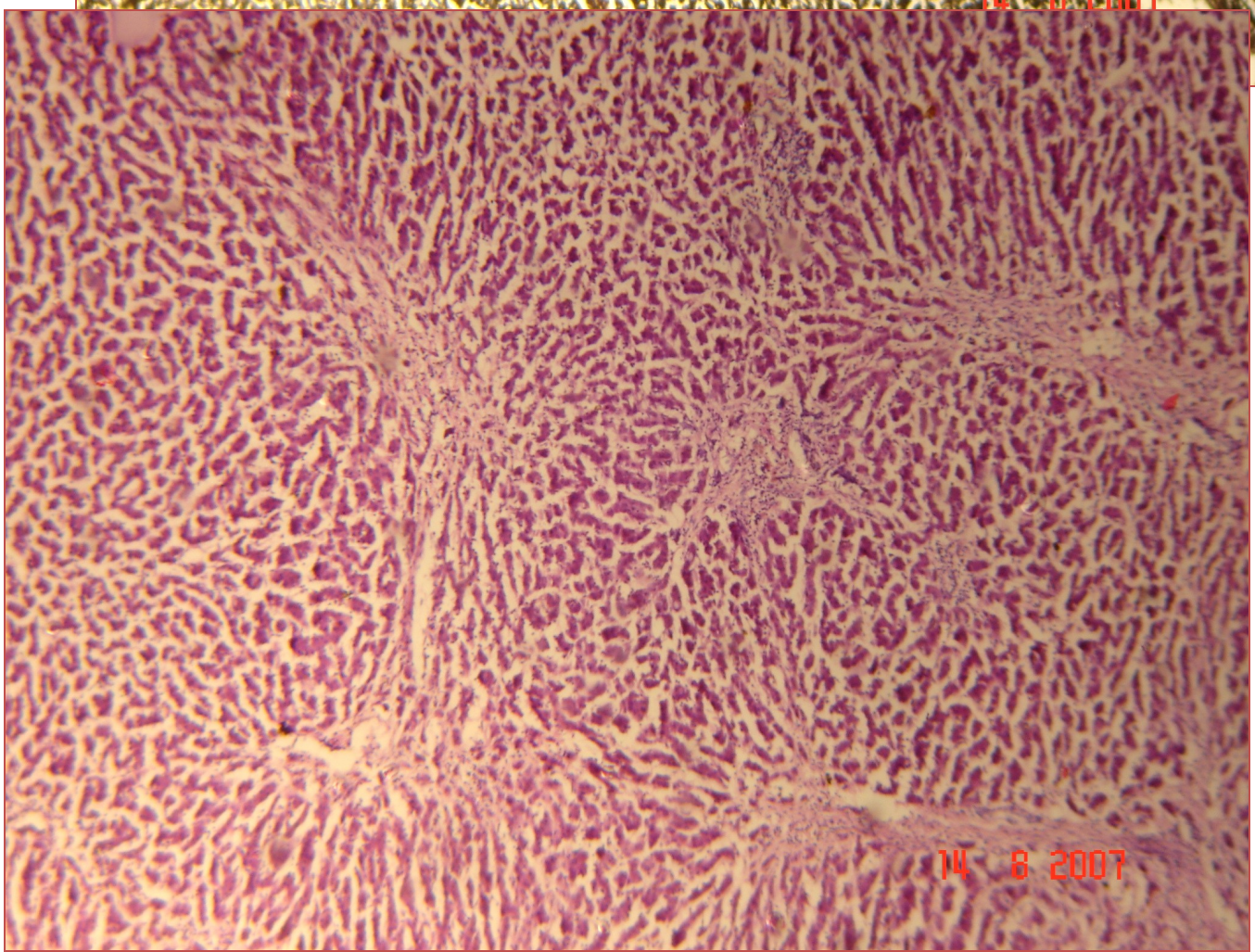

14 8 2007

Fig 12 - Bridging fibrosis low power(100x)

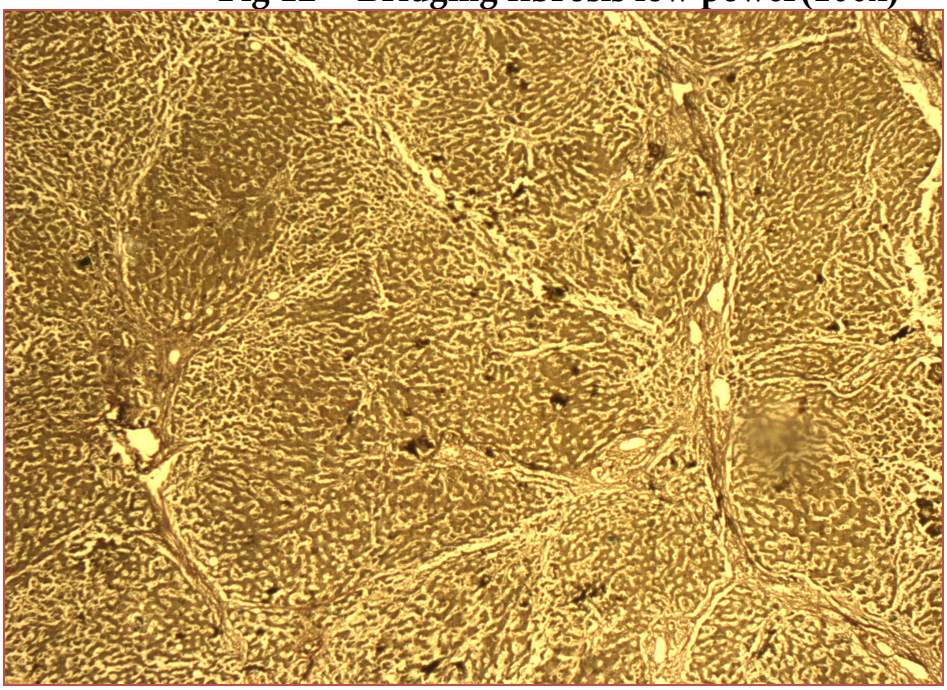


Fig 13 - Bridging fibrosis Reticulin stain – low power(100x)

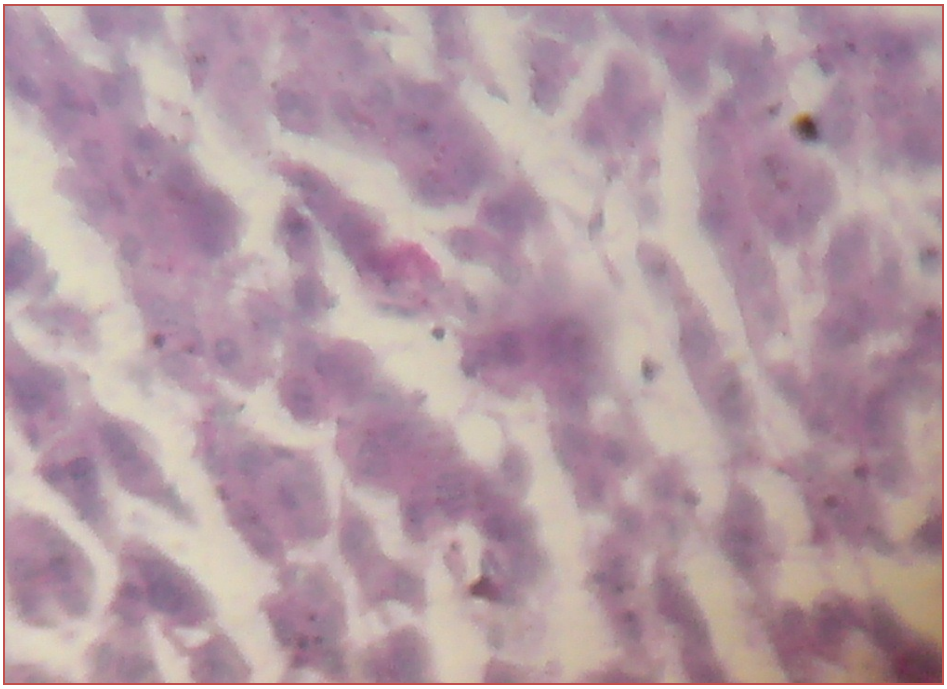


Fig 14 - Mallory hyaline – high power (450 x)

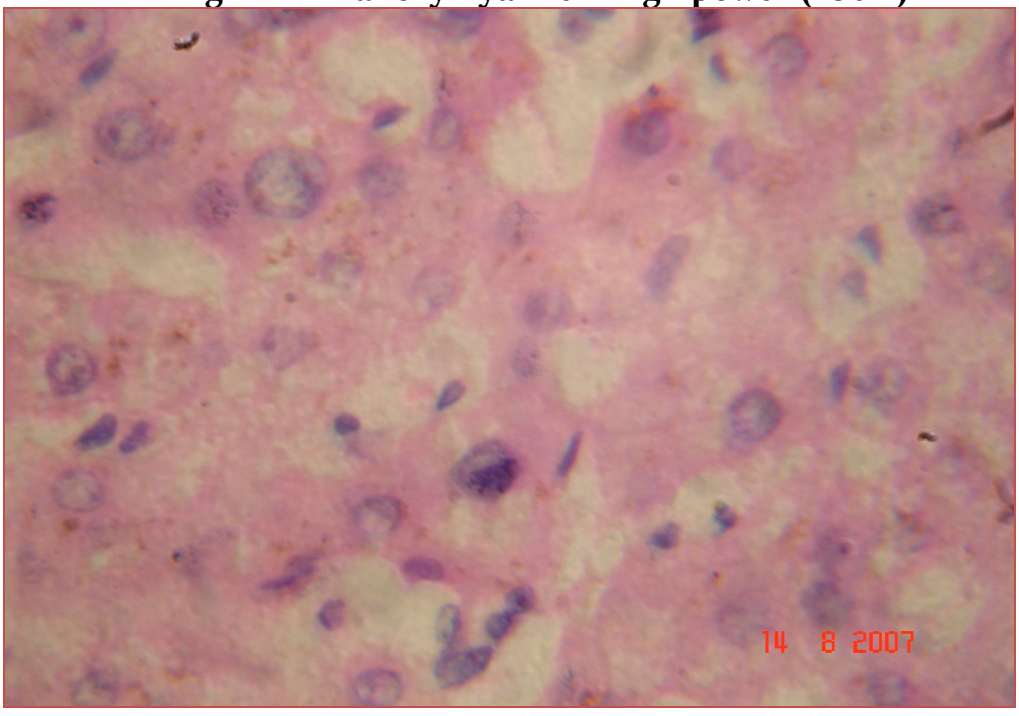


Fig 15 - Ground glass hepatocytes - high power(450x)

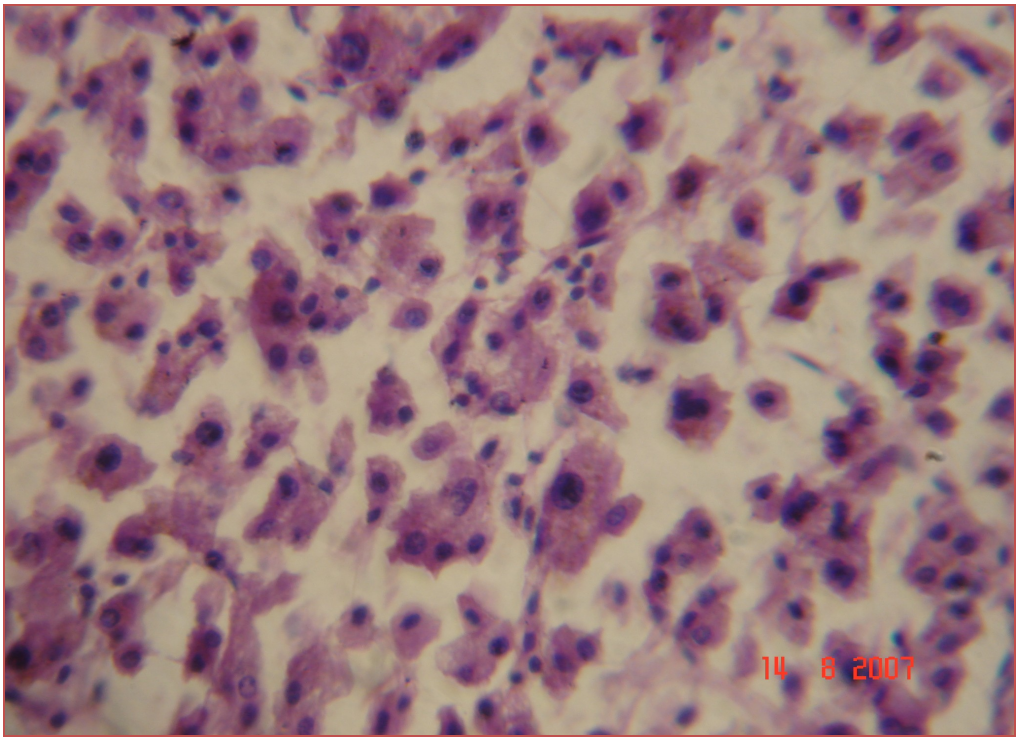


Fig 16 - liver cell dysplasia - high power(450x)

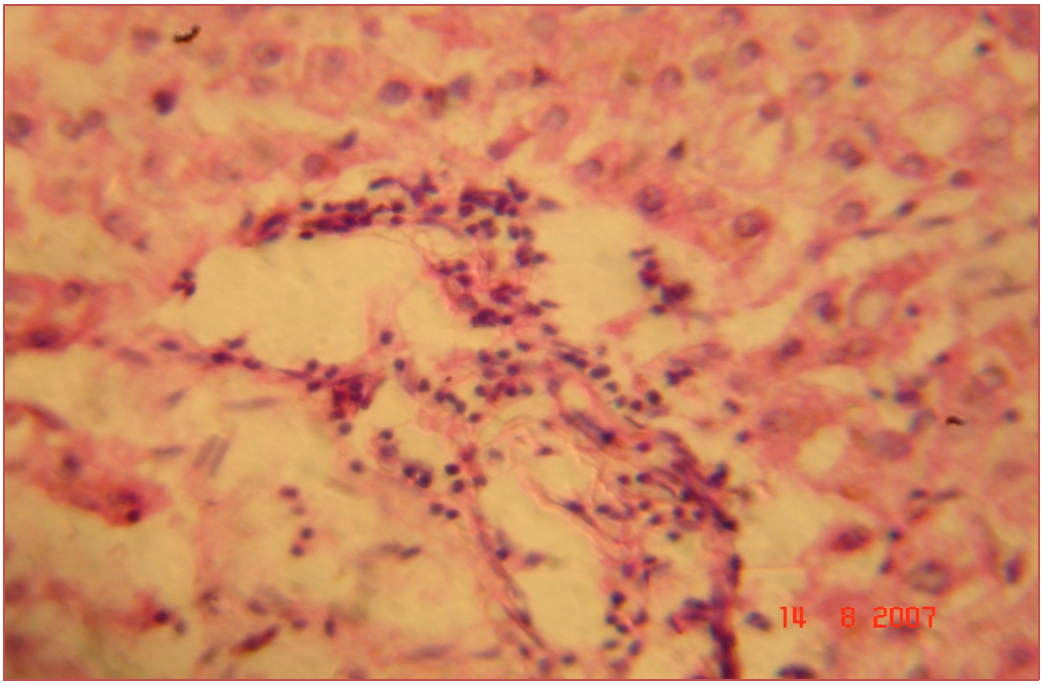


Fig 17 - hepatocytes with ballooning degeneration and portal inflammation high power (450x)

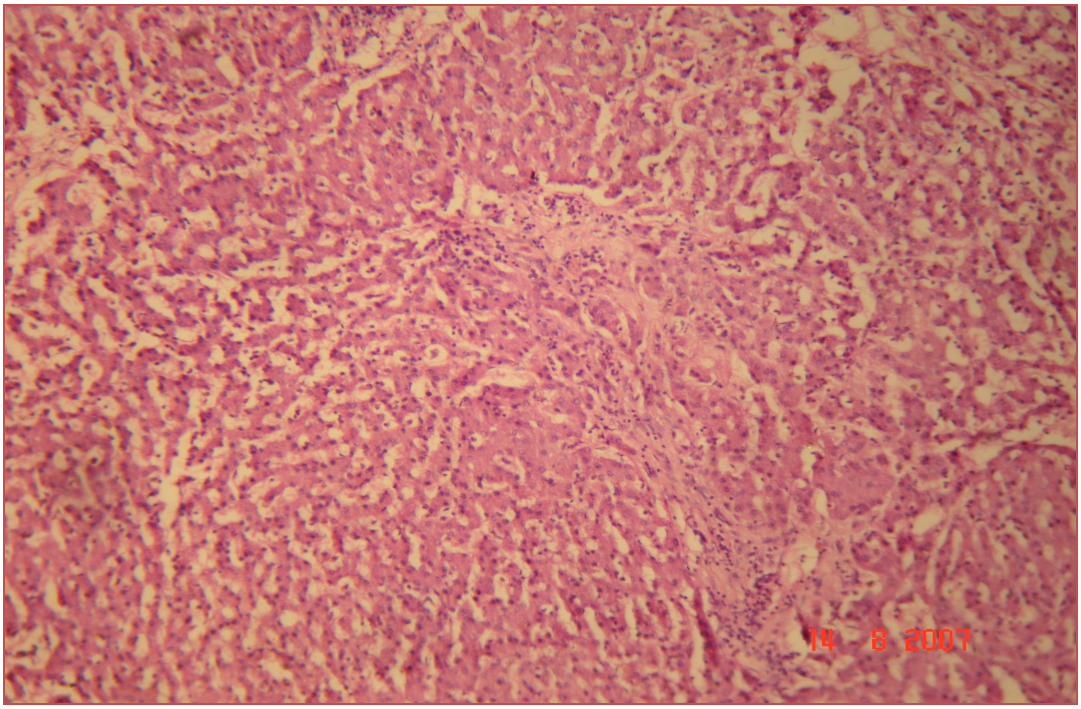


Fig 18 - portal and acinar inflammation – low power

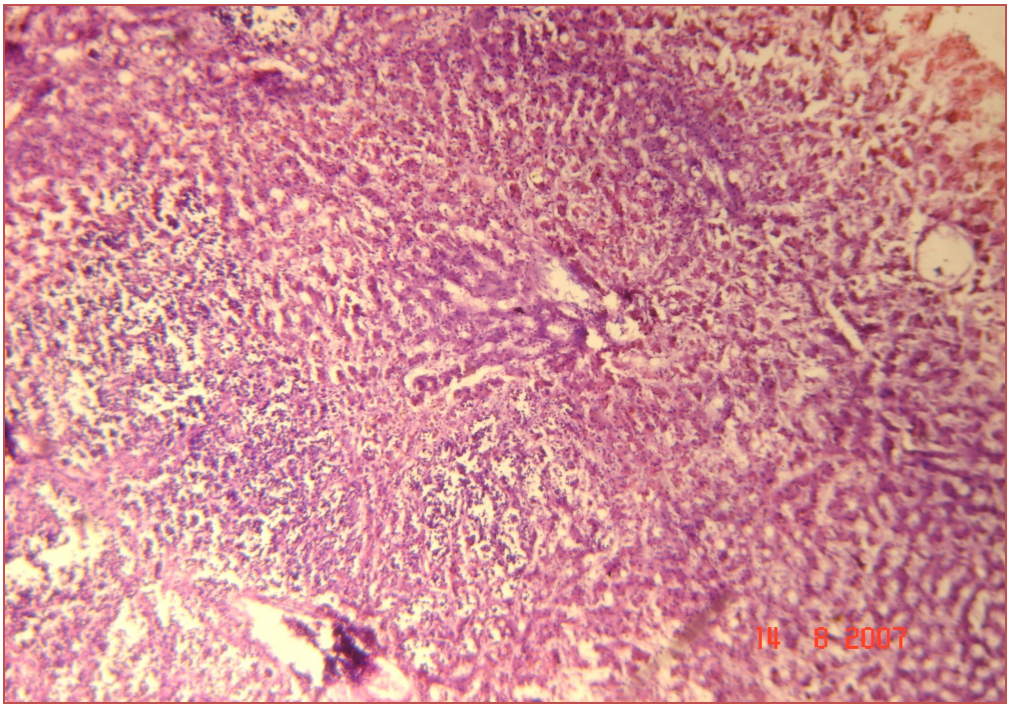


Fig 19 - metastatic adenocarcinomatous deposit – low power

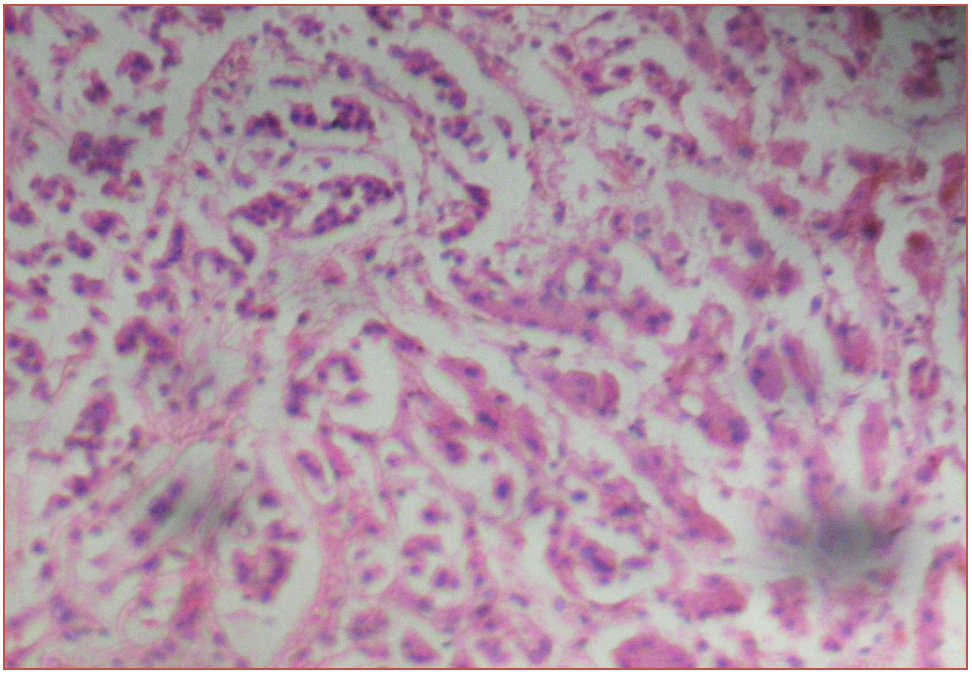
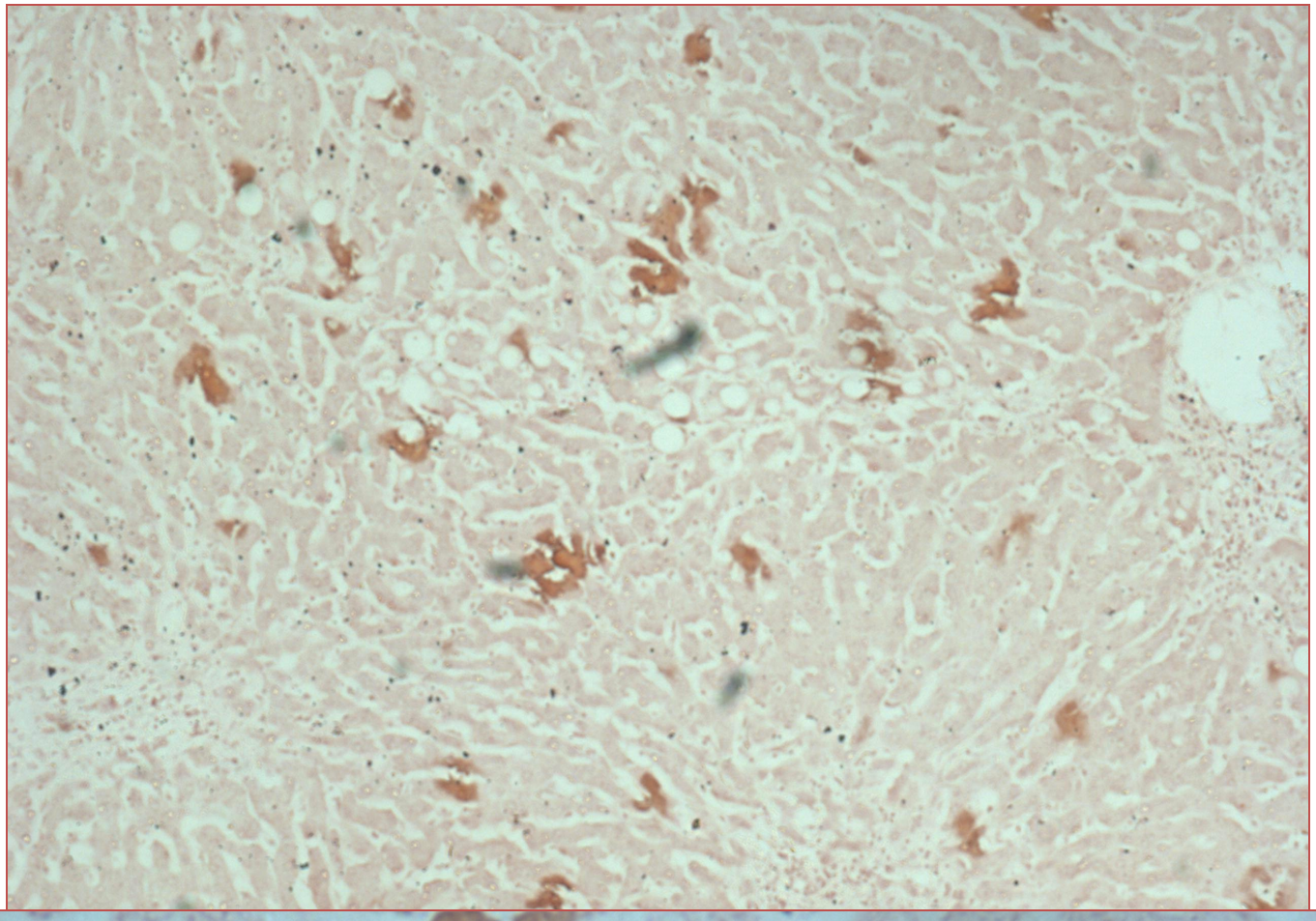


Fig 20 – metastatic deposits- breast - low power(100x)



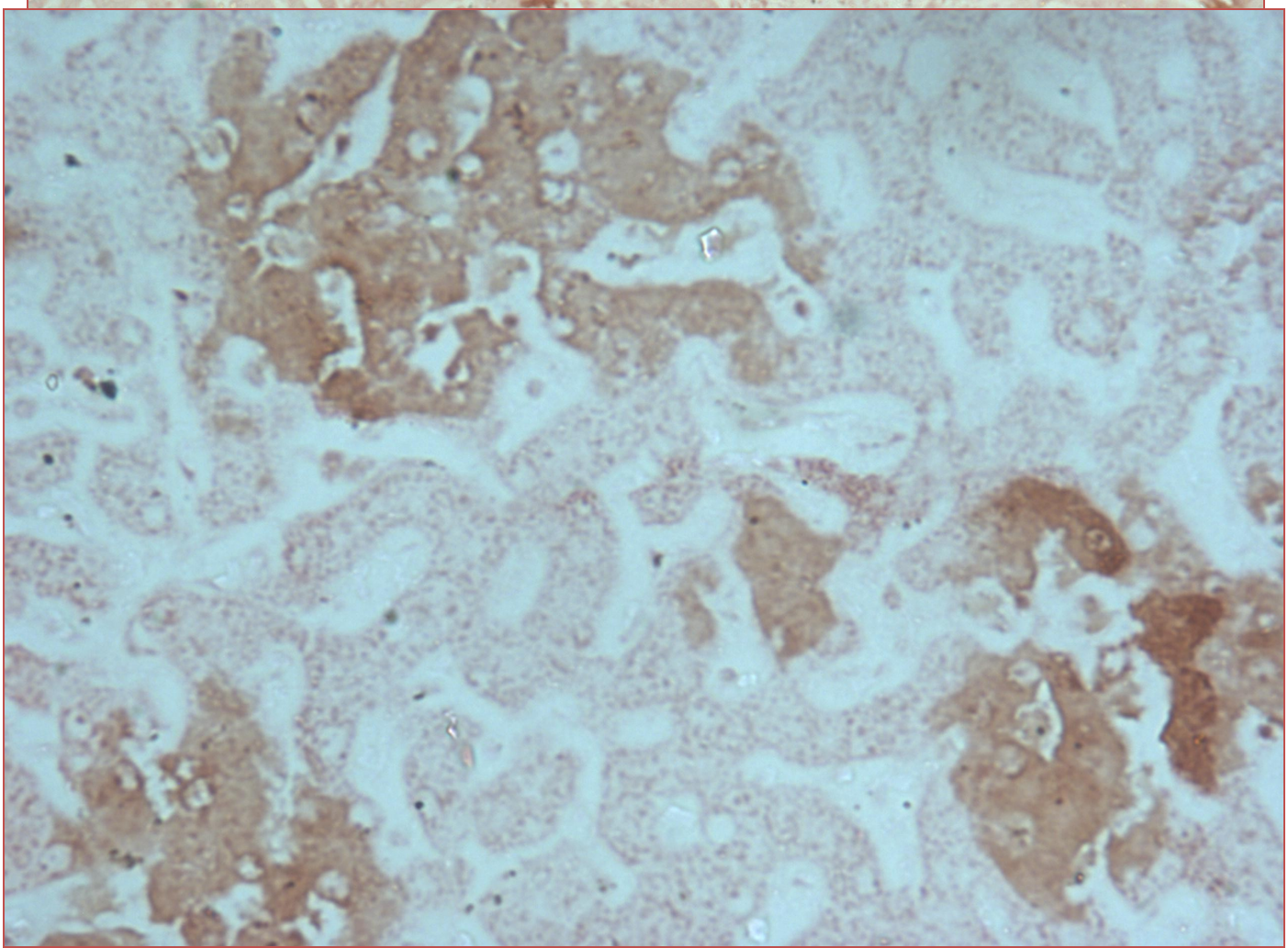


Fig 22-Positive staining Ground glass hepatocytes in clusters- ORCEIN stain High Power (450x)

SUMMARY and CONCLUSION

SUMMARY AND CONCLUSION

This study takes into account of the available data ie. age, sex and cause of death, histological features and special staining in arriving at the following observations: No clinical data what so ever was available.

Out of the 77 cases among the males, 49.3% were of normal histology,19.5% were steatosis,13% were chronic venous congestion liver, 6.5% were due to steatohepatitis,5.2% were cirrhosis,3.9% were chronic hepatitis,1.3% was due to metastatic disease and 1.3% showed features of liver cell dysplasia.

Out of the 23 female cases,47.8% were of normal histology,13% was due to steatohepatitis,8.7% were steatosis, 8.7% were chronic venous congestion liver, 13% were chronic hepatitis, 4.4% was due to metastatic disease and 4.4% showed features of liver cell dysplasia. There were no cases of cirrhosis in females in the study.

1. Based on histological and supportive orcein staining we observed hepatitis (Hepatitis B) in 14 cases (14%).

2. Steatosis was observed as early as 22 yrs of age.

3. Cirrhosis was noted only among the male population in our study.

4. Liver cell dysplasia was evident mainly in the elderly candidates.

5. Earliest phase of chronic venous congestion, chronic hepatitis and steatohepatitis were noted as early as in the fourth decade.

6. Cirrhosis was observed as early as in the fifth decade.

7. Steatohepatitis was noted in three females without history of alcoholism probably suggesting these to be cases of non alcoholic steatohepatitis(NASH).

This study reiterates the importance of the clinical autopsy in understanding the magnitude of clinically silent liver lesions. A substantial percentage of cases were found to be harboring hepatitis which would have far reaching consequences both clinically and socially.

The high incidence of NASH among the female population shows that metabolic syndrome among women continues to be under diagnosed.

The study also highights the unexpectedly high prevalence of steatohepatitis among the younger generation.

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Annexure

MASTER CHART

i

S.NO	Age	PM No.	Cause	GROSS		Morphological features														
	Sex			Weight	Nodules	steatosis	Necrosis				Inflammation		Fibrosis			Nodules	Sinusoidal	GGH	Ballooning	ch st
							Confluent	Piecemeal	Bridging	Centriobular	Portal	Acinar	Portal	Bridging	Pericellular		congestion		degeneration	
1	45/M	229/07	FALL	1000gm	-	-	-	+	-	-	+	-	+	+	-	+	-	+	-	
2	40/M	232/07	Natural	1350 gm	-	++	-	-	-	-	-	-	-	-	-	-	-	-	-	
3	55/F	233/07	RTA	1600gm	-	+	-	-	-	-	+	+	+	-	+	-	-	-	+	
4	45/F	249/07	RTA	1200gm	-	-	-	+	-	-	+	-	+	+	-	-	-	-	-	
5	60/F	250/07	RTA	1100gm	-	-	-	-	-	-	-	+	-	-	-	-	+	+	-	
6	49/M	253/07	RTA	1300gm	-	-	-	-	-	+	-	-	-	-	-	-	+	-	-	
7	63/M	254/07	RTA	900gm	+	+	-	+	-	-	+	-	+	+	-	+	-	-	-	
8	40/F	255/07	Hanging	1200gm	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	
9	51/M	256/07	Natural	1800gm	-	++	-	-	-	-	-	-	-	-	-	-	-	-	-	
10	40/M	259/07	Poisioning	1200gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
11	39/M	262/07	Fall	1600gm	-	++	-	-	-	-	-	-	-	-	-	-	-	-	-	
12	38/M	263/07	RTA	1550gm	-	-	-	-	-	+	-	-	-	-	-	-	+	-	-	
13	60/M	264/07	RTA	1100gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
14	50/M	293/07	RTA	1100gm	-	-	-	-	-	-	+	+	-	-	+	-	-	+	+	
15	40/M	294/07	RTA	1200gm	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	
16	55/F	299/07	Natural	1800gm	-	-	+	-	-	+	-	-	-	-	-	-	+	+	-	
17	28/F	300/07	Poisioning	1200gm	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	
18	60/M	302/07	RTA	1300gm	-	++	-	-	-	-	-	-	-	-	-	-	-	-	+	
19	42/M	303/07	RTA	1400gm	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	
20	50/M	304/07	RTA	1800gm	-	-	-	-	-	-	+	-	-	-	-	-	+	-	-	
21	60/F	305/07	RTA	1200gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-		

ii

S.NO	Age	PM No.	Cause	GROSS		Morphological features														
	Sex			Weight	Nodules	steatosis	Necrosis				Inflammation		Fibrosis			Nodules	Sinusoidal	GGH	Ballooning	ch st
							Confluent	Piecemeal	Bridging	Centriobular	Portal	Acinar	Portal	Bridging	Pericellular		congestion		degeneration	
22	50/M	308/07	Natural	1300gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
23	34/F	309/07	Poisioning	1100gm	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	
24	38/F	314/07	Natural	2200gm	-	++	-	-	-	-	+	+	-	+	+	-	-	-	-	
25	35/M	311/07	RTA	1100gm	-	-	-	-	-	-	+	-	-	-	-	-	+	-	-	
26	65/M	314/07	Natural	1200gm	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	
27	49/M	319/07	RTA	1500gm	-	-	-	+	-	-	+	+	-	+	-	-	-	-	+	

28	30/M	338/07	RTA	1800gm	-	++	-	-	-	-	-	-	-	-	-	-	-	-	-	
29	35/F	337/07	Fall	1800gm	-	+	-	-	-	+	-	-	-	-	-	-	+	-	-	
30	55/M	339/07	RTA	2200gm	-	++	-	-	-	-	-	-	-	-	-	-	-	-	-	
31	70/M	341/07	RTA	1500gm	-	-	-	-	-	-	+	-	-	-	-	-	+	-	-	
32	50/M	343/07	RTA	1200gm	-	+	-	-	-	-	+	-	-	-	-	-	-	-	-	
33	60/M	344/07	RTA	1400gm	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	
34	75/F	345/07	RTA	1500gm	-	-	-	-	-	-	+	+	-	-	-	-	+	-	-	
35	50/M	347/07	RTA	1400gm	-	-	-	-	-	+	-	-	-	-	-	-	+	-	-	
36	50/F	348/07	Natural	1200gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
37	50/F	350/07	Natural	1800gm	-	-	-	+	-	-	+	+	+	+	-	-	-	+	+	
38	52/M	354/07	RTA	1400gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
39	50/F	355/07	Fall	1300gm	-	++	+	-	-	-	+	+	-	-	+	-	-	+	+	
40	56/M	356/07	RTA	1600gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
41	28/M	357/07	Fall	1200gm	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	
42	35/F	368/07	Natural	1200gm	-	-	-	-	-	+	+	-	-	-	-	-	+	-	-	
43	48/M	379/07	RTA	2000gm	-	-	-	-	-	+	-	-	-	-	-	-	+	-	-	
44	60/M	383/07	Fall	1500gm	-	-	-	+	-	-	+	-	+	+	-	-	-	-	-	
45	54/M	384/07	Fall	1800gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

S.NO	Age	PM No.	Cause	GROSS		Morphological features													
	Sex			Weight	Nodules	steatosis	Necrosis				Inflammation		Fibrosis			Nodules	Sinusoidal	GGH	Ballooning	ch st
							Confluent	Piecemeal	Bridging	Centriobular	Portal	Acinar	Portal	Bridging	Pericellular		congestion		degeneration	
46	45/F	387/07	Natural	1400gm	-	-	-	-	-	-	+	-	-	-	-	-	+	-	-	
47	24/M	388/07	RTA	1500gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
48	21/M	390/07	Fall	1600gm	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	
49	64/M	395/07	RTA	1600gm	-	++	+	-	-	-	+	+	-	-	+	-	-	-	+	
50	38/M	394/07	RTA	1600gm	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	
51	22/M	396/07	RTA	1400gm	-	++	-	-	-	-	-	-	-	-	-	-	-	-	-	
52	22/M	400/07	Fall	1200gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
53	26/M	401/07	RTA	1550gm	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	
54	23/M	402/07	RTA	1250gm	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	
55	20/M	403/07	RTA	1600gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
56	50/M	414/07	Fall	1600gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
57	45/M	415/07	RTA	1800gm	-	+	-	-	-	+	-	-	-	-	-	-	-	-	-	
58	35/M	418/07	Natural	1650gm	-	++	-	-	-	-	-	+	-	-	-	-	+	-	-	
59	77/M	419/07	RTA	1800gm	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	
60	28/M	432/07	RTA	1850gm	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	
61	48/M	431/07	Fall	1450gm	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	
62	60/M	435/07	RTA	1750gm	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	
63	55/M	436/07	Poisioning	1500gm	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	
64	23/F	437/07	Poisioning	1400gm	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	
65	38/M	441/07	RTA	1550gm	-	++	+	-	-	-	+	+	-	-	-	-	+	-	-	
66	31/M	442/07	RTA	1850gm	-	++	-	-	-	-	-	+	-	-	-	-	+	-	+	
67	40/M	443/07	Fall	1500gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
68	38/M	444/07	RTA	1300gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
69	28/M	445/07	RTA	1300gm	-	-	-	-	-	+	-	-	-	-	-	-	+	-		

S.NO	Age	PM No.	Cause	GROSS		Morphological features													
	Sex			Weight	Nodul-es	steatosis	Necrosis				Inflammation		Fibrosis			Nodules	Sinusoidal	GGH	Ballooning	ch st
							Confluent	Piecemeal	Bridging	Centriobular	Portal	Acinar	Portal	Bridging	Pericellular		congestion		degeneration	

70	56/M	448/07	Fall	1700gm	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-
71	33/M	457/07	RTA	1200gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
72	21/M	459/07	RTA	1300gm	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-
73	50/M	460/07	Hanging	1400gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
74	50/F	462/07	Natural	1800gm	-	+	-	-	-	-	-	+	-	-	-	-	-	-	-
75	70/M	461/07	RTA	1000gm	-	-	-	-	-	-	+	-	+	+	-	-	-	-	-
76	59/F	464/07	Burns	1200gm	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-
77	35/M	465/07	RTA	1400gm	-	++	-	-	-	-	-	-	-	-	-	-	+	-	-
78	55/M	466/07	RTA	1300gm	-	++	-	-	-	-	-	-	-	-	-	-	-	-	-
79	50/M	467/07	RTA	1200gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
80	35/F	468/07	RTA	1600gm	-	-	-	+	-	-	+	+	-	-	-	-	-	-	+
81	61/M	473/07	Fall	1600gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
82	80/M	477/07	RTA	1400gm	-	-	-	-	-	-	-	+	-	-	-	-	-	+	-
83	40/M	484/07	RTA	1650gm	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-
84	38/M	483/07	RTA	1300gm	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-
85	40/M	508/07	RTA	1400gm	-	++	-	-	-	-	-	-	-	-	-	-	-	-	-
86	50/M	513/07	Fall	1700gm	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-
87	79/F	515/07	RTA	1600gm	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-
88	40/M	523/07	RTA	1200gm	-	+++	-	-	-	-	+	+	-	-	+	-	-	-	+
89	50/M	539/07	Fall	1850gm	-	++	-	-	-	-	+	-	-	-	-	-	-	+	-
90	55/M	540/07	RTA	1400gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
91	70/M	542/07	RTA	1100gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
92	54/M	543/07	Natural	1200gm	-	-	-	-	-	-	+	-	-	-	-	-	+	-	-
93	48/F	544/07	RTA	1400gm	-	-	-	-	+	-	+	-	-	+	-	-	-	-	+

S.NO	Age	PM No.	Cause	GROSS		Morphological features														
	Sex			Weight	Nodules	steatosis	Necrosis				Inflammation		Fibrosis			Nodules	Sinusoidal	GGH	Ballooning	ch st
							Confluent	Piecemeal	Bridging	Centrilobular	Portal	Acinar	Portal	Bridging	Pericellular		congestion		degeneration	
94	50/M	548/07	RTA	1650gm	-	-	-	-	-	+	-	-	-	-	-	-	+	-	-	
95	50/M	555/07	RTA	1650gm	-	+++	-	-	-	-	+	+	-	+	+	-	-	-	+	
96	65/M	564/07	RTA	950gm	+	+	-	-	+	-	+	-	+	+	-	+	-	-	-	
97	58/M	566/07	RTA	1350gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
98	54/F	567/07	RTA	1400gm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
99	60/M	569/07	RTA	1550gm	-	++	-	-	-	-	-	-	-	-	-	-	+	-	-	
100	58/M	570/07	RTA	1500gm	-	++	-	-	-	-	-	-	-	-	-	-	-	-	-	

PROFORMA

NAME:

AGE/SEX:

PM NO.:

DISS.No.:

CAUSE FOR PM:

GROSS: THE LIVER (gm) HAS A SHARP/ BLUNT MARGIN.

SURFACE IS INTACT/ SMOOTH/ GLISTENING/ OTHERS.

PARENCHYMA IS RED- BROWN/YELLOW WITH USUAL

/ ACCENTUATED/ OTHER LOBULAR PATTERN

NODULES PRESENT/ ABSENT.

MICROSCOPY:

H AND E STAIN

RETICULIN

PERLS'

ORCEIN

PAS

REMARKS